INTRA-UTERINE CONTRACEPTION

PROCEEDINGS OF THE

SECOND INTERNATIONAL CONFERENCE

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Edited by

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and
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EDITORS' FOREWORD

The Second International Conference on Intra-Uterine Contraception sponsored by The Population Council was held in New York City on October 2-3, 1964. The registration of more than 400 included representatives of thirty-eight countries, public health officers of many states and municipalities, observers from several international agencies concerned with technical assistance to developing countries, and virtually all clinical and laboratory investigators concerned with the subject of intra-uterine contraception. When the attendance at this conference is compared with the 48 participants, mostly observers, at the first conference in 1962, it is obvious that the 1962 meeting was eminently successful in bringing the subject to the attention of the medical community. Scores of research projects all over the world were begun following the first conference. Our call for abstracts in early 1964 brought far more than could be placed on the program of a two-day conference.

In undertaking the combined tasks of organizing the program of this conference and editing the proceedings, we have had the invaluable consultation of our colleagues on The Population Council's Advisory Committee on Intra-Uterine Contraception. Dr. Howard C. Taylor, Jr., Chairman of this Committee, served also as Conference Chairman. His skillful guidance made it possible to present twenty-seven papers from the platform, and still allow ample time for vigorous and pertinent discussions from the floor. In providing a thoughtful and thought-provoking summary, Dr. Alan Guttmacher contributed in a much appreciated manner to the success of the conference. The other members of the Committee, Dr. Nicholson J. Eastman, Dr. Kenneth A. Laurence, and Dr. Christopher Tietze, were of equal importance in carrying out a successful conference.

These proceedings include the full text of all papers presented at the conference, a condensed transcript of the discussion, and additional papers and abstracts of work that could not be included in a program that was limited to two days. Since the value of the published proceedings of such a conference diminishes rapidly as new work clarifies or solves many of the problems discussed, the editors have made every effort to achieve early publication. They have made some minor changes in arrangement and phraseology of the manuscripts submitted and have condensed and rearranged the verbatim transcript of discussions from the floor, but in all cases the editors have striven to preserve the experimental data and the intention and essence of the point of view of all participants. To conserve time, edited copy was not submitted to the participants for approval; the editors, therefore, must take full responsibility for any errors that may appear in spite of their best efforts.

S. J. SEGAL A. L. SOUTHAM K. D. SHAFER

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INTRODUCTORY REMARKS

by

JOHN D. ROCKEFELLER 3rd,* FRANK W. NOTESTEIN,** and
CHAIRMAN HOWARD C. TAYLOR, Jr.***

MR. ROCKEFELLER: It is a pleasure and a satisfaction for me to welcome you to this meeting today. I appreciate your being here, and particularly we are grateful to those of you who have come very long distances.

Personally, I believe that the problem of unchecked population growth is as urgently important as any facing mankind today. Until recently, I believed an even graver problem was the control of nuclear weapons. However, there is a justifiable hope that the use of these weapons can be prevented; but there is no hope that we can escape a tremendous growth in world population. Therefore it becomes a central task of our time to stabilize this growth soon enough to avoid its smothering consequences.

In this effort bio-medical scientists like yourselves have an extremely important role to play. Your knowledge and wisdom can help guide and direct governmental policies and programs, your research findings will contribute significantly towards providing modern methodology for family limitation. Your work can thus be a major factor in the success of national family planning programs, upon which rest the hopes of many countries for economic survival and for the well-being of their people.

During the two and a half years since The Population Council sponsored the first conference on intra-uterine contraception, great forward strides have been made in this field. In consequence, this meeting can be of historic importance in applying the knowledge from modern science to a major world problem to the great benefit of mankind.

I am happy to welcome you to these meetings, both personally and on behalf of my fellow trustees of The Population Council, and I trust that you will have a most profitable and constructive exchange of information and viewpoints in the next two days.

MR. NOTESTEIN : I only want to reiterate the welcome you've already had on behalf of The Population Council and all of our colleagues in it, and in the second place, to express my special gratitude to all of you who have engaged in such a wide range of research on a topic of major importance.

Finally, I want to express the hope that just possibly this conference marks the beginning of a new era, in which for the first time in history we may see the practical chance of controlling population in ways that remove it as a major obstacle to the achievement of health, education, and prosperity for all the world's people. This indeed will be science in the service of humanity.

You are all most welcome.

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Chairman TAYLOR: It is hardly necessary to point out the importance of this conference. The large attendance is irrefutable testimony to the significance being attributed to the gathering. I would like to say therefore just a few words about some of the things the conference should hope to accomplish.

The development of a collaborative project for the study of the intra-uterine device, before its final recommendation for widespread use, has been consistent with the modern and rational approach to problems intimately concerned with the public health and social welfare. Never before perhaps has a similar project been planned and carried out with such conscientious caution and foresight. The participants in this conference must continue to carry a considerable responsibility on their shoulders.

The contributions in our program are individual ones reporting the experiences and impressions of single workers and of small groups. Nevertheless it is hoped that when the conference is over certain general facts will become available that will allow us to draw some general conclusions.

The work of the conference will be concerned with organization and with means of bringing information to the people of various countries, and with the development of services. Doubtless no type of organization will be found to be universally applicable, but we should arrive at certain patterns known to be effective and perhaps learn of others that are not so successful.

We will also be concerned with side reactions and possible complications. It is time that we should know rather precisely the frequency of failures, the incidence of unpleasant symptoms and the chances of accidents, and face directly the issue of whether the advantages from these devices clearly outweigh possible hazards. Finally, the means by which the device exercises its contraceptive action is important, both for its scientific interest and its significance with respect to certain philosophical and, indeed, theological principles.

We are beginning our sessions with a sense of the enormous importance of the subject matter and of our own responsibility. I dare to hope that we will be able to conclude with a sense of progress made and a clearer, perhaps more substantiated, view of the place of the intra-uterine device in the solution of what seems to be the world's most pressing problem.

HISTORICAL REVIEW OF INTRA-UTERINE DEVICES

by

ANNA L. SOUTHAM, M.D.[*]

The use of intra-uterine devices to influence fertility is an ancient technique. For centuries, Arabian and Turkish camel owners have used intra-uterine contraception to prevent pregnancy in their saddle animals. Their technique was simple. A small stone (pessary) was inserted into the uterus through a hollow tube. It is believed that Aristotle was referring to this technique when he recommended the castration of camels in preparation for crossing the desert.[1]

The first mention of intra-uterine pessaries in ancient medicine occurs in the Hippocratic writings on "Diseases of Women". A hollow lead sound was passed into the uterus and used for their insertion.[8] For over 2,000 years intra-uterine devices have been used for every conceivable reason, including population control. Many different materials have been utilized. These include wool, ivory, wood, glass, silver and gold, ebony and pewter; they have been made of platinum and studded with diamonds.

The nineteenth-century literature on intra-uterine pessaries is voluminous. They were used chiefly for the correction of supposed uterine displacement, but also for contraception.[6,11] The older literature on stem pessaries has some relevance to the use of modern designs. Heated discussions on the safety and efficiency of intra-uterine devices and reports on their merits or their ill effects filled pages of the transactions of gynecological societies in the United States, in France, Germany, and the British Isles. The list of patents issued for new designs was long and each inventor claimed that his device was safer, more effective, and easier to insert. The same questions arose that face us now. Various materials were evaluated. The importance of choosing the proper size and design was noted. Contraindications to the use of intra-uterine devices were defined; the chief contraindication was infection and all advocates carefully excluded women with adnexal disease from their series. The question of cancer was raised; many reports of removal of foreign bodies from the uterus years after their insertion are noted. A single report of cancer associated with a stem pessary has been found and this is in no way documented.[15] The devices did not produce sterility.

Waves of enthusiasm followed by storms of protest continued into the twentieth century, when their use for the prevention of conception was stressed. In 1916[3] and again in 1921[4], Robert L. Dickinson predicted that some very simple, completely intra-uterine device would eventually be adopted for birth control. The Pust intra-uterine ring[10] with a cervical extension and the completely intra-uterine ring of Gräfenberg[5] finally replaced earlier designs, and their introduction marked the beginning of a new era.[13]

Gräfenberg, in 1929, reported on a series of over 2,000 insertions of silkworm or silver intra-uterine rings. The failure rate with the silver ring was only 1.6 percent. Careful microscopic study of endometrial tissue was carried out in collaboration with Professor Robert Meyer. No signs of inflammation were found. Gräfenberg felt that silver rings caused an increase in the functional activity of the endometrium and that gold rings caused less hypersecretion than silver. Both Gräfenberg and Pust stressed the fact that neither device should be used in women with pelvic inflammatory disease, but Gräfenberg did not consider simple cervicitis as a contraindication to insertion. There was some disagreement between Pust and Gräfenberg about design. Pust felt that the simple cervical extension on his silkworm ring was an advantage. Gräfenberg insisted that any cervical extension was ill-advised. This question as it concerns our modern devices is as yet unanswered. The Seventh International Birth Control Conference in 1930 considered intra-uterine contraception at some length. It was stressed that neither the Pust nor Gräfenberg design has any similarity to the earlier rigid uterocervical stems, which were condemned. Further scientific appraisal of the promising method was suggested but did not immediately materialize.[12]

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In 1959 Oppenheimer[9] from Israel reported on his many years of experience with modifications of the Gräfenberg ring. His series included 1,500 cases and he encountered no serious complications. Ishihama,[7] also in 1959, reviewed the results obtained with the use of the Ota ring in 20,000 Japanese women. Japanese workers were the first to utilize nonreactive, inexpensive, plastic materials for intra-uterine contraceptive devices. These two reports renewed interest and stimulated further research. Seen in the light of the alarming rate of population growth, the need for a simple, effective method of birth control demanded reevaluation of this old technique and led to the first international conference on intra-uterine contraceptive devices just 2½ years ago. At that time, reports from Japan, Israel, Egypt, Taiwan, Chile, Puerto Rico, England, and the United States indicated that intra-uterine devices were being effectively used in many parts of the world.[14] Provisions were made for carefully controlled scientific observations on the efficiency, the safety, and the mode of action of the intra-uterine contraceptive devices. The worldwide cooperative scientific effort which followed is unparalleled in the evaluation of any method of birth control.

I would like to close with a quotation concerning intra-uterine devices from the writings of an eminent British gynecologist and surgeon: "This instrument has gone through the vicissitudes of fortune, experiencing in turn the highest encomiums and the most sweeping condemnation. Yet it has never been forgotten.... Notwithstanding the opposition it still encounters, chiefly from those who have never used it, and who consequently do not understand the subject, it is at the present day more in favour than at any previous time." George Granville Bantock's summary on the status of intra-uterine devices, written in 1884, adequately describes the situation today.[2]

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PART I

FIELD TRIALS, CLINICAL PROGRAMS, AND STATISTICAL EVALUATION OF INTRA-UTERINE CONTRACEPTION

APPLICATION OF INTRA-UTERINE CONTRACEPTION IN FAMILY PLANNING PROGRAMS

by

BERNARD BERELSON, Ph.D.*

At the first international conference on intra-uterine contraception, held less than two and a half years ago, there were 48 people in attendance from 11 countries, and the papers were given exclusively by doctors engaged in experimental clinical study of the device. Today, at this conference, there are ten of us in attendance for every one in May 1962, from four times as many countries, and many people here are concerned with the applicability of the device in national programs to implement family planning. This increase in interest serves to introduce what may fairly be described, I think, as a truly revolutionary development in enabling mankind to deal with the major world problem of undue population growth.

At the outset of this meeting it is important for us to appreciate the dramatic progress that has been made over the past two and a half years—indeed, as we shall see, even in the past several months. A rough estimate is that in May 1962, at the time of the first conference, the number of newly developed intra-uterine contraceptive devices (IUCD) being used throughout the world was somewhere in the hundreds; today this figure is in the vicinity of 100,000, and we are only at the beginning. Then we had perhaps a few thousand woman-months of experience with the newly developed plastic devices; today we have hundreds of thousands. Then we had small, typically clinical, programs in a very few countries; today we have programs of various sizes, including three virtually national ones, in over 40 countries and on every continent. Then those of us concerned with implementing family planning in the developing countries were eagerly looking for a contraceptive method with such ideal characteristics as high effectiveness, good safety, single application for a long period, easy reversibility, a simple supply system, low cost; today we may have it. In my own view, the problems of introducing contraception into the typical populations of the developing countries have become substantially easier of solution, and our prospects of success correspondingly better, now that this device is available.

I shall attempt to provide a quick survey of the field use of intra-uterine contraception. There is a kind of natural history in introducing the IUCD into a national family planning program, with five distinguishable steps or stages:

Stage One: Governmental officials and the medical community learn that such devices have been experimentally developed and are being used by reputable colleagues elsewhere. This stage, it must be noted, is marked by some suspicion and even disbelief, given the traditional medical opinion of such devices.

Stage Two: A few doctors, not officially connected, begin to experiment with the device in their private practices or through the facilities of private family planning organizations.

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* Vice President, The Population Council.

Such practice seldom accumulates large numbers of patients but it does provide direct clinical experience with the device, and puts some empirical evidence in the scale against traditional medical opinion.

Stage Three: Clinical researchers with a direct or indirect governmental association undertake systematic inquiry into the safety and effectiveness of the IUCD under local conditions, the local side effects and complaints, etc. This is, of course, a necessary development; each medical community and responsible governmental office must make its own investigations and come to its own decisions. The study may go forward under the immediate auspices of a governmental maternity hospital or a city health department or the obstetrical clinic of a medical school, and it is often supervised by a special medical advisory committee set up for the purpose, including some of the country's leading obstetricians and gynecologists. Since such a device depends upon the good opinion of the medical community, it is obviously important to develop an informed medical judgment as early as practicable.

Stage Four: This is characterized by the extension of the program from the closely controlled medical clinic to the larger experiment or demonstration, to test the broad acceptability of the device and its performance under normal field conditions. This requires the training or retraining of obstetricians and gynecologists in insertion of the device and related matters. To this date, virtually all the devices in field programs have been inserted by doctors who have specialized in obstetrics and gynecology. However, at least one country is now studying an extension to general practitioners in areas where no obstetricians and gynecologists are available.

Stage Five: Large-scale plans are made to set up administrative machinery for inserting the device on a national or near-national scale—no longer as medical testing or field experimentation but as a family planning service program in its own right. Such plans vary widely according to local circumstances— they may be carried out via health stations, planned parenthood clinics, private obstetricians, postpartum clinics in hospitals, even mobile teams. But once determined and tested out, the effort "goes national" along the indicated lines as a service program of family planning.

I do not wish to claim, in view of the complexity and magnitude of this problem, that everything flows as neatly and logically as these categories may suggest, but at the same time there has been a rough progression along those lines—a natural history, and one that takes some time. However, given a genuine decision to do something effective about a country's population problem, given a reasonably open-minded medical community, given a workable administrative authority, given adequate funds, and given no political obstacles, a country can move through these stages in two years or less. At least, a few countries have done so.

At the present time, the countries of the developing world range across this continuum. Only a few have moved all the way to Stage Five, but several countries are working their way in that direction.

The earlier conference and the publication of its proceedings provided this development a certain amount of visibility in the world medical community, and no doubt the present conference will hasten if not complete the informational task itself, that is, Stage One. With regard to Stage Two it is impossible to say precisely how widespread the use of modern IUCD is through private channels, but certainly there now are thousands of doctors involved in at least 40 countries.

The whole matter becomes much more consequential when a country moves into Stage Three, with an inquiry conducted in a governmental institution and often under direct governmental auspices and with an official medical advisory committee. To date in the developing countries, this stage has been reached or passed by Korea, Taiwan, Hong Kong, Malaysia, Pakistan, India, Ceylon, Fiji, Chile, Venezuela, Jamaica, Puerto Rico, Barbados, Egypt, Tunisia, Nigeria, Ghana, and Southern Rhodesia.

The fourth stage, of large-scale field demonstrations to test acceptability by the mass of the people, has been entered upon by Korea, Taiwan, and Hong Kong, and it appears highly likely that at least three or four other countries will do so within the next several months (including one country not yet mentioned, Turkey, which is awaiting the expected repeal of certain legal restrictions before moving ahead rapidly in this field).

Finally the last stage of nationwide implementation of a service program is just now being undertaken by those same three countries—Korea, Taiwan, Hong Kong—each of which is now beginning its own manufacture of the device itself (the Lippes loop).

It is appropriate, I think, to make two observations about this review of recent developments—and both are contained in the very phrase itself. First, this whole story is very recent: rarely has so much been done on so complex a medical and administrative front in so little time. Second, the story is developmental: no country has turned back once it has genuinely begun an active and substantial effort in this field. No medical advisory committee, once confronted with its own national experience, has disapproved the provision of intra-uterine contraception to its own people. The local experience has always confirmed the existing international experience.

This trend can be documented in the accumulated data. As of September 1, 1964 here are the total number of insertions in those countries from Stage Three with 1,000 or more insertions:

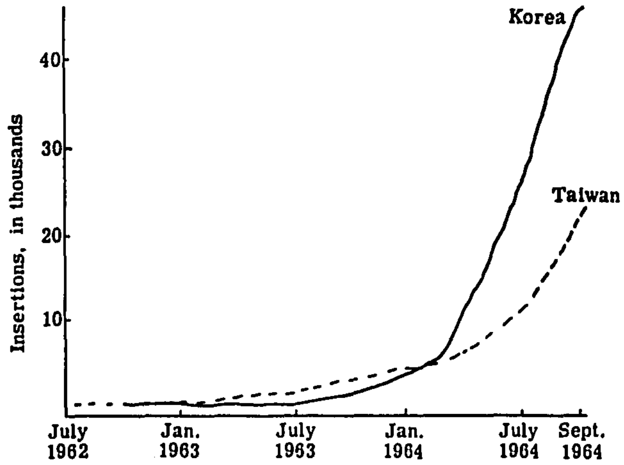
Korea (began program in September 1962)	50,647
Taiwan (July 1962)	24,742
Chile (October 1959)	6,415
Pakistan (December 1962)	4,800 (approx.)
Hong Kong (June 1963)	4,048
India (September 1962)	2,000 (est.)
Puerto Rico (November 1961)	1,531

In addition, up to 700 have been inserted in each of the other countries, including some that began their programs only a few months ago, e.g., Jamaica (April 1964) with 688, or Tunisia (July 1964) with 200 to 250 (plus others as noted in the abstracts). For comparative purposes, the 33 United States centers in the cooperative statistical program of the National Committee on Maternal Health report a total of 16,200 insertions to September 1, 1964, and there are probably some thousands more in this country that are not included in that program. In addition, there are study programs now under way in such developed countries as Australia, Denmark, England, Japan, New Zealand, and Sweden.

Thus, as a conservative estimate, there are now well over 100,000 IUCD in current use—and this despite the fact that qualified doctors and clinical hours have everywhere been limited: there has not yet been a maximum effort anywhere in the world. If the targets of the various countries' programs for December 31, 1964 are reached, as seems altogether likely, the next three months will see the total of insertions rise by at least half again. On September 1, 1964, then, the grand total of woman-months covered by intra-uterine contraception, in rough figures but to indicate order of magnitude, was close to half a million.

What may be more important than these absolute numbers, impressive though they are under the circumstances, is the trend they represent. As of one year ago, in September 1963, these same programs had accounted for less than 10 percent of this total; and even six months ago, on March 1, 1964, the figure was only about 20 percent of this total. Back in May 1962, at the first conference, about 1,000 cases with the new plastic devices were reported in the

United States and only about 125 abroad, all in Puerto Rico. This great increase is largely due, of course, to the greatly accelerated activity in Korea and Taiwan. Here is what can happen when a country decides to move ahead along this line—again with severe limitations operating in each case. So far as is known, no other contraceptive method has ever shown an acceptability record of this kind.



The programmatic means by which this development has come about reflect a great heterogeneity of local circumstances: private physicians, planned parenthood clinics, governmental health stations, medical school clinics in obstetrics-gynecology, postpartum clinics in maternity hospitals, public health centers, mobile clinics. The device has been inserted either free to the patient or, outside the U.S., at fees mainly ranging from $0.20 to $0.75.

It remains for me to say something of the women themselves, the acceptors of IUCD. As nearly as we can now tell, they do not represent any particular segment of the community, not even the women of high parity. They appear to come in substantial numbers from all parts of the population—another encouraging sign for the use of the device. In Jamaica, Chile, and Hong Kong they are mainly urban women, but in Taiwan, Puerto Rico, and Pakistan half are from the rural areas. In Taiwan, Korea, and Pakistan large proportions have had no formal schooling and are illiterate. In age and parity, the encouraging fact is that the device is accepted early enough to make an appreciable difference in completed fertility:

	Percentage of users under 30 years of age	*Percentage of users with three or fewer children*
Puerto Rico	72%	56%
Chile	49%	40%
Hong Kong	37%	38%
Jamaica	63%	35%
Korea (approx.)	25%	35%
Taiwan	28%	29%
Pakistan	52%	21%
United States	(not estimated)	66%

In short, the device does not seem to be unattractive or unusable to any substantial class of women in the developing countries: older and younger, educated and uneducated, literate and illiterate, urban and rural, even lower as well as higher parity—all appear to accept intra-uterine contraception. Across the world, they have been accepted by members of every race and of several major religions—Protestants and Jews, Catholics and Buddhists, Moslems and Hindus. And wherever the device has been offered in direct competition with other contraceptive methods, as with the so-called "cafeteria choice," it has gained at least as many acceptors as any other method, and usually more (up to 80 percent in Taiwan).

As a behavioral scientist in this distinguished gathering of medical men, I would like to pay my respects to those people who have developed and tested the various intra-uterine devices. Concerned as I am with implementing family planning programs in the field, I can testify to the great value of having available a contraceptive method of this character. If in this conference you confirm the value of this device from the medical standpoint, and if the next two and a half years see a continuation of the progress of the past, then we shall be successfully on the road to an historically important, even unique, accomplishment. In many environments this method may well signify the difference between success and failure in family planning programs and hence it represents, at least potentially, a tremendous contribution to the welfare of individual families and national communities, with all that this means for the economic prosperity, the political stability, and the freedom of mankind. Indeed, I believe that this simple device can and will change the history of the world.

THE PROGRAM FOR INTRA-UTERINE CONTRACEPTIVE DEVICES IN TAIWAN: DEVELOPMENT, SETTING, AND EVALUATION†

by

T.C. HSU, M.D.*, L.P. CHOW, M.D.** and S.M. KEENY, M.A.***

Taiwan has a population of 12 million in 14,000 square miles, largely mountainous. During the past 17 years the population has increased 4 percent à year (including immigration). The current rate of increase is about 3 percent. It has been estimated by our economists that Taiwan's economy can become self-supporting only if the natural increase can be reduced to about 1.5 percent a year. The need for an effective and inexpensive contraceptive method is thus obvious.

The new intra-uterine devices (IUCD) seem to offer an answer. A program to evaluate their use has been under way for two years, with encouraging results.

Intra-uterine contraception is not altogether new in Taiwan. A Japanese ring (the Ota ring) has been in wide use for more than 20 years. A recent survey in various parts of the country, of 8,032 married women aged 20-39 years, indicated that 23.3 percent of the respondents have practiced contraception; of these, 34.4 percent were ring wearers at one time or another.

Introduction of the new IUCD

The Margulies spiral and the Lippes loop were first introduced into Taiwan in early 1962. A study to measure the acceptability, effectiveness, and side effects of the devices was started in Taichung city in February 1963, with assistance of The Population Council. This study revealed high acceptability: of a total of 4,155 cases registered for contraception during a nine-month intensive educational campaign, 3,071 cases or 74 percent elected to use the new IUCD when offered a choice of all methods. Some other preliminary results of the study were reported in *The Scientific American* of May, 1964. The results of the medical follow-up studies will be the subject of a separate presentation. (See page 23-Ed.)

The extended family planning program

In January 1964 the program was extended to include a total of 100 townships in 15 counties and cities (out of the 361 townships in 22 counties and cities in Taiwan), with a population of 4.5 million. The townships selected were those with obstetricians and gynecologists (OBG) available, since it was planned to limit the insertion of devices at first to OBG doctors only. Training these doctors is, of course, a prerequisite for the program. There are 300 in the area, of whom 250 have received training. (*A note on the training of doctors follows the text of this paper, page 20-Ed.*)

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To educate and motivate women, 100 village health education nurses (VHEN) have been employed, organized into 30 teams of 3 persons each, with 10 supervisors. Each team is assigned to stay in a village (average population about 2,000) for one month, teaching both sanitation improvement and family planning.

Every woman who expresses the desire to have a device inserted is given a coupon which entitles her to a 50 percent discount on the cost, which is fixed at NT $ 60 (US $ 1.50). The Maternal and Child Health Association (MCHA) pays one half, the patient one half.

The extended program, although one of action, has a built-in research component. Before insertion of the device, a short questionnaire is filled out by the VHEN's for samples of women in the village. It covers attitude to, knowledge about, and practice of contraception, as well as the reproductive history and personal characteristics of the individual. Simple information, such as the type of person who referred the case and the characteristics of the case, is also entered on the coupon issued to the patient. Both sets of data are coded and transferred to IBM cards for analysis.

In each of the 100 townships one of four different "treatments" is carried out. These vary in method and intensity of coverage, from simply holding small group meetings, to individual contacts with one eighth of the women in a township by the VHEN's. Each township has, on average, 15 to 35 villages; each village has 20 to 25 Lins; and each Lin has about 15 families. The average population of one township is about 35,000, of whom 11 percent are married women 20-30 years of age.

Evaluation of the program will be made on the number and characteristics of acceptors, effort and cost, interval between the first approach and actual insertion, the type of person who referred the cases, and of course the actual decline in fertility. The study is in progress, and preliminary results for the first six months will soon be available. Some of the data may be reported at this time :

How many acceptors in 1964 ? From January 1 through August 31, a total of 21,291 women accepted the method. The monthly rate of increase has been very sharp, as shown in Figure 1.

Most (93 percent) of the acceptors were from the 15 counties or cities selected for the program; of these, 53 percent were from the townships where the VHEN's have been assigned and 47 percent from other townships. Among those from the VHEN's townships, 31 percent came from the villages where the VHEN's have actually worked, and 69 percent from other villages. Only 15 percent of the acceptors came as a result of direct contact with VHEN's; the remaining 85 percent came because of other influences, including the "circulation effect" of the program.

Who referred the cases ? Most of the cases were referred by five major types of personnel: the 100 VHEN's, the 120 pre-pregnancy health workers (PPH) who had originally been employed to promote traditional methods in 120 townships, the regular staff in the local health facilities, the private OBG doctors, and private midwives. Part of the reason for the large returns from the PPH workers is that they have on their casebooks many women who are desperately in need of more effective methods. Acceptors by sources during the month of August, exclusive of Taichung City, are given in Table I.

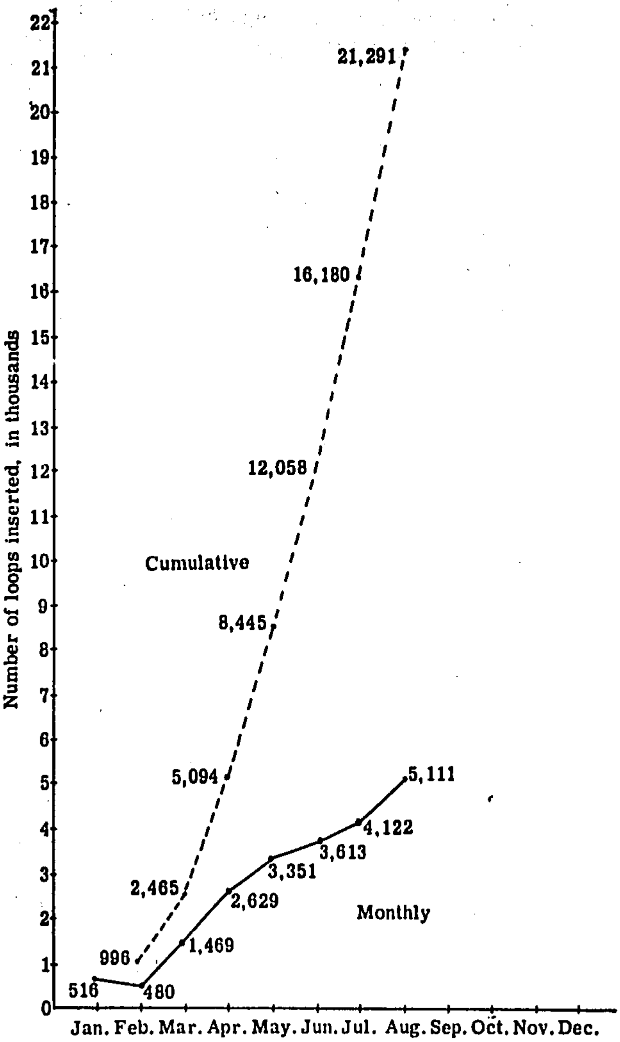

Fig. 1. Loops inserted in Taiwan (including Taichung) in 1964, by month.

TABLE I

Cases referred by	*Number*	*Percent*
Pre-pregnancy health workers	1,796	38.2
Private OBG doctors	1,562	32.4
Health Dep't stations	654	16.6
Village health education workers	336	6.6
Others	301	3.2
Private midwives	110	2.2
Not clear	65	0.8
Total	4,824	100.0

What types of women accepted devices? As might be expected, women of higher parity are the first to accept the method in the initial stage of the program. The mode of parity among acceptors was 4 living children (25.8 percent) and 2 sons (38.8 percent); the mode of age was 30-34 years (35.7 percent).

Follow-up survey on samples of acceptors and coupon holders. Acceptors are told by the doctors to come back for medical check-up at the first, third, and sixth month after insertion. Most women, however, do not come back unless they have some trouble. The magnitude of the program makes it impracticable for the health workers to pursue every case for follow-up examination. For evaluation of the program, it has been decided that follow-up interviews will be completed with only a sample of the acceptors. Public health nurses in the Taiwan Population Studies Center are doing these follow-up interviews.

Questions asked during the follow-up interview reveal whether the device has been removed or expelled; whether pregnancy has occurred; whether there were any side effects; from whom or where the woman first heard about the device; who influenced the woman most in her decision to have a device inserted.

An interview survey will also be made on samples of women who said they would accept the IUCD and were therefore given coupons but have not used them. This survey is designed to reveal the reasons that prevent these women from having the loops inserted.

A pre-test has been made on 193 women in a township near Taichung City. Interviews were completed with 136, or 70 percent, of these women. Out of 32 acceptors, 2 had already removed the device because of discomfort, 2 had expelled it, 1 is not certain; the remaining 27 cases are presumably continuing users. Twenty cases, or 63 percent, had no complaints; the other 12 cases had some complaints, mostly minor; 78 percent of the acceptors said the device is satisfactory. Each acceptor claimed to have persuaded friends to accept the device; the average number of friends so persuaded is 2.2.

"Wait and see" was the most frequent reason given for delay. An additional push by workers may help these women to act.

The follow-up survey has been under way since early September. Analysis of the data, including samples of clinical records of OBG doctors, will be made soon. Our preliminary impression is that the method is equally welcome to women in Taichung City and in the rural areas. Women in Taiwan are ready to accept a contraceptive method that is inexpensive and requires little attention, so that direct contact with only a segment of women will be enough to promote the program. Information spreads by word of mouth with surprising speed. Small group meetings also appear to be a reasonably inexpensive way to get cases.

Other field experiments

Three subsidiary field studies of smaller scale in connection with the IUCD program are under way. One is the group meeting study, which will measure the effectiveness of holding small group meetings to encourage women to accept the method.

The second study will measure the effectiveness of the distribution of printed leaflets to motivate rural women to accept intra-uterine contraception.

The third study is the use of non-OBG doctors for insertion of the loop, and payment of a small reward to those who may refer cases. A fishing area with 45,000 people but without an OBG specialist has been chosen for the study.

Traditional methods versus the IUCD

The 120 pre-pregnancy health workers mentioned above have registered, during the past few years, 50,000 cases to practise the traditional methods. Immediately after the implementation of the extended program described in this paper, many of the acceptors of traditional methods shifted to the IUCD. The cumulative total of such cases reached 2,188 by the end of July. Preference for intra-uterine contraception over traditional methods may be seen from this quick response.

Further extension of the experimental pre-pregnancy health program

New developments have just taken place. Although there has been no official policy statement, there has been rapid growth of informal support among leaders of the community and the public. Newspapers now carry information about the program almost every day.

It is planned that 140 additional workers will be employed to bring the number of program workers up to 360, to cover all of Taiwan. For areas where there are no OBG doctors, selected general practitioners or doctors in the health stations will have to be appointed; plans are under way to meet the new requirement.

The rapid expansion of the program will require many more devices and inserters. Local products approved by The Population Council will be available in October, 1964, at about one third of the U.S. cost.

These developments follow the recent request of the economic planning body that the action program be accelerated to bring down the birth rate more rapidly. On its request, projections have been made of the future population of Taiwan, based on present trends without the intensive family planning program, and alternatively based on the intensive family planning program with intra-uterine contraception as the chief method. NT $ 30 million (US $ 750,000) are being made available for the insertion of 600,000 loops in five years. The expected achievement of the program is shown by the following projections of population trends in Taiwan with and without attempted control.

TABLE II

	Without FP program	*With FP program*	*Difference*
Population of Taiwan (1,000's)			
1963	12,117	12,117	—
1973	15,396	14,756	640
1988	22,890	19,552	3,338
Annual Live Births (1,000's)			
1963	424	424	—
1973	488	354	134
1988	686	453	233
Crude Birth Rate			
1963	36.3	36.3	—
1973	31.7	24.0	7.7 (24.3%)
1988	30.0	23.2	6.8 (22.7%)
General Fertility Rate			
1963	170	170	—
1973	134	98	36 (26.9%)
1988	126	88	38 (30.2%)
Natural Increase			
1963	30.2	30.2	—
1973	26.6	18.7	7.9 (29.7%)
1988	24.0	17.3	5.7 (23.8%)

ACKNOWLEDGEMENT

The authors wish to acknowledge the valuable contributions of their colleagues on the Taiwan Pre-pregnancy Health and Population Studies Project.

Thanks are especially due to Dr. S.C. Hsu, Chief, Rural Health Division, Sino-American Joint Commission on Rural Reconstruction, for his cooperation and assistance.

ADDENDUM

TRAINING OF DOCTORS FOR THE IUCD PROGRAM IN TAIWAN†

by

L.P. CHOW, M.D.* and C.H. LEE, M.D.**

There are about 5,000 practising doctors in Taiwan, of whom about 500 are specialists in obstetrics and gynecology (OBG). In order to initiate the program for intra-uterine contraception in Taiwan as carefully as possible, the Provincial Department of Health decided that, in the first stage, only OBG doctors should be allowed to insert the devices. Organization and training of OBG doctors was thus a prerequisite for the program. This was undertaken by the series of actions described below.

Training of OBG specialists from the government hospitals

In Taiwan there are 17 provincial general hospitals, one provincial women's hospital, 9 county or city general hospitals, and one city women's hospital. The chief obstetricians of these hospitals were first called to Taichung to attend a two-day seminar and to practice insertions. A total of 36 OBG specialists participated. The subjects covered in the seminar included:

1. *Population problem of Taiwan*: Participants were told of probable consequences of current population trends in Taiwan. The main purpose was to arouse their sense of responsibility to the community.
2. *Medical follow-up study of the IUCD* : The preliminary results of the medical follow-up study of the new IUCD were then given. It was explained that, in one case in every five, the device would not be satisfactory but complaints would be mostly minor. Building up confidence in patients would solve most of the troubles, but in a minor proportion of the cases, with rather severe side effects, removal might be indicated.
3. *Current status of fertility control and oral contraceptives*: Participants were also exposed to the knowledge about the current status of fertility control in other parts of the world. This included the traditional methods and the oral pills. It was surprising to find that OBG doctors in Taiwan had only superficial knowledge about contraceptive methods.
4. *Research procedures*: Since we like to encourage research on the use of the new IUCD, research procedures are explained. Attention was drawn to possible biases in comparing the effectiveness of contraceptive methods. For example, the diaphragm tends to be more effective than the foam tablet simply because more educated women elect to use it. In

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† This supplementary paper was not presented at the conference.

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addition, the computation of pregnancy rates, the minimum number of cases and length of observation required for reliable data, and the method of tabulation and analysis of study results was also introduced.

5. *Work procedures of the program*: Explanation of the work procedures of the program, including referral of cases, clinical record forms, coupons, charges for insertion, and working relationships with the local practitioners, etc., was given.
6. *Clinical instruction and practice*: The participants were given clinical instruction and an opportunity to witness at least two insertions and to perform one. Movies ("The Magic Mortar," and "New Intra-Uterine Plastic Contraceptive Devices") were shown, followed by a question-and-answer period. Generally, these OBG doctors did not find the insertion of the new IUCD difficult, because all of them have had much experience with the Japanese Ota ring.

Setting up demonstration clinics at government hospitals

After the seminar, all the hospitals listed above were requested by the Provincial Health Department to establish demonstration clinics, with at least one session every week. The local health departments and health stations were requested to refer cases to these clinics. The demonstration clinics serve a twofold purpose: to reinforce the training and build up the confidence of the trained OBG specialists, who would be the consultants to the private OBG practitioners in the area, and to serve as a training field for the latter.

Organization and training of the private OBG practitioners

Before the start of the IUCD program in an area, the private OBG doctors there are given a day's training. The local health director calls the meeting. Wherever possible, the demonstration clinic is used. The authors of this paper conduct the training. Cases are enlisted by the health department for clinical instruction and practice. The content of the training is a condensed and simplified version of that described for the hospital OBG specialists.

Each OBG practitioner observes at least one insertion and does one himself. Although they have had much experience with the Ota ring, they are still concerned about the possible occurrence of serious side effects, such as heavy bleeding. They are assured that such cases will be rare, and that unnecessary removals for minor complaints can usually be avoided by reassuring the patient. The question of possible infection by the nylon thread of the loop is often raised. The legal liability to perform induced abortion at the request of IUCD wearers when accidental pregnancy occurs is another major concern of these practitioners. The advisability of obtaining the consent of husbands before inserting the loops is also often discussed. The private practitioners in Taiwan are extremely cautious about legal liability for malpractice when complicated cases are encountered; they want the health authorities to give them reasonable assurance and protection.

After the OBG practitioners have attended the required training sessions, and agree to the conditions set forth by the Maternal and Child Health Association (MCHA), contracts between the two parties are signed. The charge for insertion, fixed by the MCHA at NT $ 60 (US $ 1.50), is lower than they might charge for the insertion of the Ota ring. However, they understand the importance of the program and are willing to support it. Of course there are some exceptions who require time-consuming persuasion.

Up to the end of August, training was given to 279 OBG doctors; 235 of these are in private practice, the other 44 are connected with the health services of Taiwan, mostly in provincial, county, or city hospitals.

There are 134 townships (or districts in large cities) with OBG practitioners in Taiwan; 93 of these have at least one OBG practitioner who has been trained. The intra-uterine contraception program in these 93 townships has already been started.

Study on the use of general practitioners

In the 361 townships in Taiwan there are many remote and rural areas where the need for this service is particularly serious but no OBG doctors are available. General practitioners must be trained to do insertions in these areas. To study the feasibility of this, one general practitioner of rather good educational background has been given two days' training and is doing insertions. The study was started on August 15, and by the end of August he had inserted 27 loops without much difficulty. The preliminary impression is that the use of general practitioners will be feasible, given adequate supervision.

Plans for the future

The expanded experimental pre-pregnancy health program in Taiwan has the goal of 600,000 insertions in five years. To reach this goal, the following steps will have to be undertaken:

a. Of the 500-odd OBG practitioners in Taiwan, 235 have been trained. The rest will have to be trained soon.

b. About 230 townships in Taiwan are without OBG's. Training of one or two general practitioners in each of these townships is essential.

c. The Provincial Health Department wishes to avoid competing with private practitioners, and has not allowed doctors in health stations and health departments to insert devices. In some special cases, however, training of a selected number of health-station doctors may be necessary.

Hitherto, training of the OBG doctors has been conducted by the authors of this paper. With the expected expansion of the training program, it is obvious that more instructors will be needed. Use of demonstration clinics and the chief obstetricians in these clinics may solve the problem.

CONTROL OF FERTILITY IN TAICHUNG, TAIWAN, BY USING INTRA-UTERINE CONTRACEPTIVE DEVICES: MEDICAL FOLLOW-UP

by

C.H. LEE, M.D.* and P.Y. WEI, M.D.**

Introduction

The Ota ring, a modification of Gräfenberg's ring, has been popularly used in Taiwan for contraception because of its efficacy, simplicity, and low cost. The recent survey in Taichung showed that over 20 percent of the women who practiced any form of contraception wore it. Although it has high popularity, the insertion of the ring requires the dilatation of the cervical canal. In addition, its removal is sometimes difficult. To avoid these problems new intra-uterine devices, such as the Margulies spiral and the Lippes loop, have been invented.

In July 1962, the Provincial Maternal and Child Health Institute and the Taiwan Population Studies Center, with the support of The Population Council, started an experimental program of family planning in Taichung City. The initial stage lasted from February to October 1963; the follow-up and extended program is still continuing.

The objectives of the program were twofold: first, to find the most efficient method of contraception for Taiwan, and second, to enroll cases for study of the acceptability, effectiveness, and safety of the new intra-uterine devices (IUCD). A "cafeteria" service of contraceptives was provided. Three types were included: the "traditional" condom, foam tablet, jelly, diaphram, etc.; the new intra-uterine devices; and oral contraceptives. By the end of June 1964, a total of 6,868 women had been enrolled. The breakdown by contraceptive method chosen is shown in Table I.

TABLE I

Women registered for birth control, February 1963-June 1964

Methods	Number of acceptances	Percent
Intra-uterine devices	5,479	79.8
Traditional methods	1,213	17.7
Oral contraceptives	176	2.5
Total	6,868	100

About 80 percent of the women preferred the IUCD because it does not need care after insertion and calls for no expenditure month after month. Since the IUCD is so readily accepted by women, the medical follow-up of users is very important. Here we present the results of the medical follow-up study for the first year. The total enrolled was 2,040.

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Number of cases and insertions

There were 2,040 cases of initial insertion, but only 1,892 cases (92%) were completely followed at one year. The number of cases and insertions is shown in Table II.

TABLE II

Number of cases and insertions

IUCD	Cases followed	Reinsertions	Total insertions
Spiral (5)	39	—	39
Spiral (5-J)	333	47	380
Loop (No. 1)	1,440	107	1,547
Silkworm gut	80	8	88
Total	1,892	162	2,054

The age distribution of the women is shown in Table III. Women aged 26-35 comprise 64.8 percent of the cases. The median number of pregnancies and parity were 4.3 and 3.8 respectively.

TABLE III

Age distribution of cases

Age Group	No. of women	Percent
16–20	30	1.5
21–25	316	15 5
26–30	662	32.5
31–35	660	32.3
36–40	318	15.6
41–45	54	2.6
Total	2,040	100

Spontaneous expulsions

No efforts were made to fit the IUCD according to the width of the cervical canal or the length of the uterine cavity. The rate of spontaneous expulsion at the end of one year was 12.8 percent for spiral 5; 18.0 percent for spiral 5-J; 11.3 percent for loop 1; and 14.8 percent for silkworm gut. The average rate of expulsion was 12.7 percent. The significant statistical difference between spiral and loop is noted. It may be assumed that the triangular IUCD causes less mechanical irritation than the spiral one since the loop coincides with the shape of the uterine cavity. It should be stressed here that spontaneous expulsion is most likely to occur in the first three months. We consider that the spontaneous expulsions occurring in the first month are due to an irritated uterus, to the IUCD being too small, or to a loose cervical os. Eighty-seven percent of the expulsions were noticed.

TABLE IV

Rates of expulsion, removal, and continued use

IUCD	Expulsion	Removal	Continued use
Spiral 5	12.8%	41.0%	46.2%
Spiral 5-J	18.0%	26.0%	62.8%
Loop I	11.3%	22.2%	70.0%
Silkworm gut	14.8%	18.2%	82.5%
Average	12.7%	23.1%	68.8%

Removals

As indicated in Table IV, the rate of removal for spiral 5 was 41.0 percent, for spiral 5-J, 26.0 percent; for loop 1, 22.2 percent; for silkworm gut, 18.2 percent. Some significant difference was seen between spiral 5-J and loop I. Although the number of spiral 5 insertions was small, its removal rate was so high that it seems it cannot be generally tolerated by Chinese women. As was true for expulsions, removals were mostly encountered in the first month after insertion. Any side effects, such as intermenstrual uterine bleeding or abdominal pain, usually develop soon after insertion. Many women have been frightened by such symptoms. To prevent this, thorough health education after the insertion is indispensable. The adaptation of the uterus to the IUCD may play a role in this phenomenon. When the IUCD has been fitted and adapted to the uterus after the initial phase, longer usage can be anticipated.

TABLE V

Relevant reasons for removal

Reason	% of total insertions	% of total removals
Intermenstrual bleeding	7.8	33.5
Pregnancy with IUCD *in situ*	3.2	13.7
Abdominal pain	3.0	12.7
Psychological	2.3	9.7
Lumbago	0.9	4.0
Irregular menstruation	0.7	3.2
Intermenstrual bleeding with pain	0.7	3.2
Hypermenorrhea	0.7	3.2
Husband's discomfort on sexual contact	0,3	1.3
Pelvic infection	0.3	1.3
Leukorrhea	0.2	1.0
Dysmenorrhea	0.2	1.0
Cancer of cervix uteri	0.1	0.4
Not stated	0.1	0.6
Total	20.5%	88.8%

The outstanding reasons for removal are shown in Table V in order of frequency. "Relevant" cases are those complaints considered to be related directly to the IUCD and to be important. They comprised 88.8 percent of all removals. The main reason for removal, intermenstrual bleeding, constituted 33.5 percent of all removals and amounted to 7.8 percent of insertions. "Psychological" complaints, such as palpitation, loss of body weight, dizziness and fatigue, were occasionally noted among the wearers. These might be attributed either to pelvic congestion and reflex autonomic nervous symptoms or simply to some psychological factor. For such women, mostly neurotic, psychotherapy or at least reassurance must be stressed.

There were two cases of removal because of cancer of the cervix after diagnosis by Papanicolaou's test.

Pelvic infection

Many doctors are concerned about pelvic infection after the insertion of the IUCD, especially the initiation of infection through the nylon thread or tail protruding from the cervical os. The incidence of pelvic infection during one year was 0.3 percent. In our judgment, there is little danger of pelvic infection if the insertion has been aseptic.

Continuation and effectiveness of intra-uterine contraception

Although there were 12.7 percent expulsions and 23.1 percent removals, reinsertions were sometimes requested; hence the rate of continuation at the end of one year was 68.8 percent. A significant difference in continuation was present between loop I and spiral 5-J. The continuation rate of spiral 5-J was 62.8 percent; of loop I, 70 percent. The use-effectiveness of intra-uterine devices is expressed as the pregnancy rate per hundred woman-years of exposure according to Raymond Pearl. In this series, the pregnancy rate was computed in two ways: *i.e.*, pregnancy with device *in situ* (corrected pregnancy rate) and all unintended pregnancies. The corrected pregnancy rate of spiral 5-J was 3.6, of loop I, 5.3, and of silkworm gut, 2.7. The total pregnancy rate was 4.8. The effectiveness of the IUCD is related to the size of the device; the small one has a higher failure rate; the large one, a lower. The average pregnancy rate of Taiwanese women is 57.3 per hundred woman-years between 20 and 44 years of age.

TABLE VI

Pregnancy rate by type of device

IUCD	Total insertions	Woman-months of use	Average (mo.)	Pregnancy rate	Corrected preg. rate
Spiral 5	39	316	8.1	—	—
Spiral 5-J	380	2,958	7.7	4.8	3.6
Loop I	1,547	14,393	9.3	6.0	5.3
Silkworm gut	88	871	9.9	2.7	2.7
Total	2,054	18,538	9.0	5.5	4.8

Papanicolaou smears

Vaginal smears were routinely taken before the insertion of the IUCD and then annually.

Two positive smears were found, out of 1,719 examined. Carcinoma *in situ* was confirmed by cervical biopsy. There were 1,087 smears taken from 1,301 continuing users, but no positive smears were found.

Endometrial biopsy

Endometrial biopsy was performed on those women who requested removal of the IUCD because of intermenstrual bleeding or other reasons (hypermenorrhea, lumbago and non-relevant causes). Our preliminary observations indicate an increased tendency to prolonged shedding of menstrual endometrium and a poor response to progesterone in the secretory phase, but the results of the histological interpretation are not yet conclusive. We hope to present this study in the future.

Conclusions

From our first year's results, we conclude that intra-uterine contraceptive devices, especially the Lippes loop, are effective, safe, and widely acceptable. The Ota ring has been extensively used in Taiwan because of its cheapness and simplicity. The new IUCD also meet this test.

We think we can improve our results by paying more attention to fitting each woman with the size of device most suitable to her. The Lippes loop I seems to be smaller than usually desirable, since the expulsion rate and pregnancy rate are higher than for the large one.*

In a large-scale campaign there is a loss of much of the important intimate relationship between doctor and patient that is found in good private practice. Through more careful training of doctors and field workers as a team we are trying to create a similar rapport with each woman.

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* A study on the use of larger loops has been started in Taichung. For a summary of preliminary results, see page 237.

THE NATIONAL INTRA-UTERINE CONTRACEPTIVE DEVICE EVALUATION PROGRAM OF PAKISTAN

by

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In December 1962 a research project on IUCD was started in Pakistan. Eleven clinics in different parts of the country participated under the coordination of the National Research Institute of Family Planning of the Government of Pakistan. The major objectives of the study were to determine fertility rates among Pakistani women using the device, the continuity of use, and reasons for discontinuation.

During the calendar year 1963, 1,734 women were admitted to the study. They are to be followed for at least one year after the first insertion of the IUCD. Data on service activities and types of women who received IUCD have been incorporated in Dr. Berelson's report. A comprehensive analysis will be made under the direction of Dr. Leslie Corsa of Berkeley, California, who set up the study.

After December 1963, women continued to be admitted to the same clinics and a dozen others in an extended IUCD study with simplified record and report systems, but with the same broad objectives and also coordinated by the National Research Institute. The total number of IUCD insertions reported prior to September 1964 is 4,800.

Doctors in Pakistan prefer the smaller sizes of IUCD in both the Lippes and Margulies types; 66 percent of the devices inserted were of the smaller sizes. This preference is most marked before a given physician has had much experience with the device. It demonstrates a medical as well as natural bias at first contact with the notion of inserting a foreign body into the uterus. There is also a tendency to ascribe unfavorable symptoms, especially bleeding, to the larger devices. Actual statistics on discontinuations, however, show no consistent relationship of size to frequency of bleeding as a serious complaint.

Pakistani women, partially because of chronic undernourishment throughout the growing years of childhood, have a small body habitus. It is possible that there is a correspondingly small uterus. We need to have better answers to a number of questions, such as: Is there a correlation between body size and uterus size? Is this correlation to body height or to body habitus? Is the variation in uterine size among multiparous women important enough to warrant giving this factor consideration in the routine procedures of IUCD insertion, such as sounding for uterine depth for selection of size of IUCD? Is it enough to rely upon the inserter guard to avoid reaching beyond the smallest expected uterine length? Is there a relationship between uterine size and parity?

An analysis of IUCD discontinuations in the study has been made but does not furnish full information on the side effects that occurred without leading to removal or expulsion of the IUCD. An analysis of all cases will be done eventually by computer. Nevertheless, the preliminary findings are of interest.

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One hundred and ninety-two women (11.1 percent) have already discontinued wearing IUCD. Those who discontinued had retained the device for an average of 4.1 months, compared with 5.8 months in the total group who received the IUCD. There was no exclusive concentration of discontinuations shortly after insertion, but the frequency dropped sharply after the third month. It is notable that one third of the women who discontinued did not wait even two months before doing so and two thirds of these had other reasons than spontaneous expulsions for discontinuing.

The rates of discontinuation by duration of use (retention span) in the total study population obviously is a more significant consideration than the mere percentage of women affected. The larger size of Lippes loops were introduced later in this study, but the data thus far does not seem to alter the gross impressions. The Margulies spirals were associated with much higher total discontinuation rates (about 11 and 28 percent of insertions of the small and regular size respectively) than the Lippes loops (7.5 and 7.1 percent for the small and regular size respectively). The high discontinuation rate of the larger Margulies device is due chiefly to spontaneous expulsions and bleeding complaints. Not one of the 18 pregnancies which have so far been reported, however, occurred with the Margulies spiral in place.

Free choice from a range of contraceptive methods was not offered, hence no reliable conclusion can be reached about the relative preference for IUCD. In some clinics two or three alternatives were offered. In most cases, the clinic personnel admittedly encouraged one particular method (usually the IUCD) over all the others, and it was chosen by 57 percent. In one parallel study in Pakistan a situation existed where one study population was given an opportunity to change from the IUCD to oral contraception, and another group to do the reverse. Approximately 50 percent of both shifted. This demonstrates merely that the women are not completely satisfied with any method that is as yet available to them and that a good many will experiment with almost any new method offered. This readiness to shop around for a new method probably does not apply to the traditional contraceptives with which they may have been more familiar.

With respect to acceptance of intra-uterine contraception, it is interesting to contrast the age distribution of the women in the Pakistan study with their parity. The modal point in age distribution is the 25-29 year group, with 30-34 almost as frequent. As for parity, on the other hand, half of the women have already given birth to six or more children, with an average of 4.8 children per woman. Whereas the age distribution has a very even normal curve pattern, the parity distribution rises in direct correlation with the number of children. Evidently, and as would be expected, women are interested in the IUCD in proportion to the size of the family already acquired. Their objective usually seems to be to maintain their present family size rather than to space pregnancies. In Pakistan a strong educational campaign is needed to bring women to seek IUCD for the latter purpose.

Except for initiation of the first eleven clinics, no effort was made in Pakistan at first to increase the number of centers doing IUCD work. The pressure came from the other end, from medical centers requesting IUCD supplies which were obtainable only through government channels. The government looks favorably upon the method, has supported IUCD work in 28 centers, and intends to broaden the scope to a national scale.

Side effects

In Pakistan the most frequent complaint about the IUCD is bleeding. Women return to the doctor asking for removal of the device even though the bleeding may be of minor degree.

Menstrual periods, especially at the beginning, may be longer and more profuse. Nevertheless, the women show great concern. This in Pakistan seems more properly to be called concern than alarm. The reasons for this are several. One is interference with a woman's daily prayers. Among Muslim women, prayers are forbidden during menstruation and no clear distinction exists among most people between menstruation and other vaginal bleeding.

Also in keeping with the religious and other connotations of uncleanness about menstruation, sexual abstinence is the usual practice. Both reasons, then, drive the women back to the clinic for removal of the IUCD. It is understandable why bleeding is reported frequently in Pakistan. It is difficult, if not impossible, to quantify bleeding. It is not surprising that undernourished women of high parity, with frequent genito-urinary infection and cervicitis, should bleed more with the IUCD. Anemic women are more sensitive to fatigue with the same amount of bleeding and therefore complain more about it. Bleeding must be considered more seriously in a population where a severe degree of anemia is common. On the other hand, it is our impression that Pakistani women relatively seldom complain of pain.

Technical aspects of insertion and follow-up

In a mass program where IUCD work necessarily is done by less competent persons, whether physicians or others, the question needs to be asked and answered concerning the amount of surgical manipulation that should be routinely permitted. Is it necessary to pass a sound for the dual purpose of determining uterine depth and direction? Is not the inserter flexible enough so that it will usually follow the axis of the uterine cavity, and will the IUCD not position itself in the cavity almost regardless of the effort of the operator to control its direction and position? How important is it to achieve the frontal plane before the device leaves the inserter? Does the device change its position over a period of time under the influence of uterine contractions? Is this tendency affected by the size of the device with respect to that of the uterine cavity. If there is difficulty passing the inserter through the cervical os, should dilatation be done? Would it not be preferable to have the woman return after the next menstrual period or be advised to use another type of contraception? In Pakistan the policy is to make the IUCD insertion a surgical procedure to the least possible extent rather than exerting every effort to place a device in women regardless of difficulties encountered.

One problem is the case where the cervical extension is not visible on speculum examination, but the woman has not noted expulsion of the device. The procedure to follow in a mass program with limited access to consultation or diagnostic service is necessarily different from that in an urban medical center. The recommended procedure in Pakistan is to insert a second device rather than try to take a diagnostic X ray. In any event, X ray should be postponed until after the next menstruation in order to avoid irradiating an early fetus. The woman should be advised to seek definitive diagnosis concerning the presence of the device if she decides at a future date that she wishes to become pregnant.

In Pakistan the large majority of the population lives in rural areas with difficult transportation and scarce professional personnel. Strong justification exists for setting up pilot studies that seek practical methods of bringing the IUCD to these people with safety by means of other types of workers trained in the method. In most countries heretofore, insertion has been restricted to physicians, or even physicians with previous gynecologic experience as a requirement for IUCD training and work. It would seem that the major requirement should be not so much the type of university degree as the past practical experience. A trained midwife with long obstetric experience would seem preferable to a physician in general practice with little or no gynecologic training or experience. On these questions, few people will raise issue. In most places the question is quite academic because the scarcity of trained midwives may be as great as the scarcity of qualified physicians. Is it reasonable to consider training a corps of IUCD workers with less medical background? It would seem desirable to do a limited study on the training needs, educability, need for supervision, and other problems encountered in a sample of such non-professional personnel. In a way, the basic question is more philosophical than medical. Aside from other factors, preference undoubtedly exists for a better rather than a less trained worker. However, the choice may be between some service and no service, or between uterine injury on the one hand and maternal and infant mortality and morbidity and other consequences of uncontrolled parity on the other. Nor can the larger social and economic picture be disassociated from the question.

Whether professional personnel for IUCD work can be brought to the more remote rural areas depends not merely on the frequency of clinic sessions for insertions but also on the need for professional service to meet the subsequent problems that may ensue. Here, the question of adequacy of follow-up supervision falls into two parts: one is the factor of urgency, the other is the level of professional competency called for. It is unlikely that there would be more than a rare emergency after IUCD insertion. The chief possibilities are perforation, hemorrhage, and infection. For all of these, if serious enough, the woman should be brought to the hospital. Therefore the availability of hospital care for serious illness is the basic question rather than the need for full-time IUCD personnel on the scene. For example, one woman in this study developed acute appendicitis.

We have encountered one case of uterine perforation. The woman had no complaints but X ray was taken because the device was not visible at the cervix. It was found lying free in the peritoneal cavity and no attempt at its removal seemed to be indicated in the absence of symptoms. The patient was ten weeks postpartum at the time of insertion and probably had incomplete uterine involution. In Pakistan it is now recommended that three months be allowed to elapse after parturition before insertion. In the study cases, the device was removed only twice because of infection. In both, findings at the time of insertion indicated that infection was already present to a degree that should have warranted postponement.

In at least four cases, hemorrhage severe enough to require hospitalization for curettage occurred. In each instance curettings were definitely indicative or strongly suspicious of pregnancy. In at least two, conception may have antedated insertion. Only larger numbers and very close attention to details of timing will tell whether IUCD insertion after conception will increase the otherwise anticipated abortion rate, and it is impossible to know when methods of inducing abortion may have been resorted to.

The second question, that of the desirable level of professional competence for follow-up observation, can theoretically be met in two directions. The need for higher level consultation calls for the same solution as discussed previously for hospital care. In a sense, an opposite arrangement can be set up. A trained person could come periodically to do the insertions, and in the intervals any medical or para-medical person not trained in insertion could be called upon to remove the device if indicated or to refer the patient to a hospital, both actions supported by guidelines established for them.

It would be interesting to experiment with a program of transporting women to a centrally located clinic for insertion rather than aiming for mobility of the clinic. For a single visit at an optional time, many women would be expected to have a fairly high degree of mobility in contrast with the closer accessibility called for in a continuous or repetitive type of medical treatment.

When a clinic, whether fixed or itinerant, is scheduled on much less than a daily basis, attention must be given to the policy concerning the time in the menstrual cycle when insertion will be permitted. Since the optimum time is generally recognized to be shortly after menstruation, a large majority of the women who come to a clinic for the first time would have to be told to come back on another date. It would not always be easy to match clinic schedule with the woman's menstrual cycle. On the other hand, permitting insertion at any time in the menstrual cycle would lead to a certain percentage of insertions after conception. In Pakistan, with an average interval of three years between births among women who come to the family planning clinics for the first time, it is calculated that at least 2 percent of the women receiving insertions at random times in the menstrual cycle would already be pregnant. This degree of risk is probably outweighed by the other arguments that warrant a liberal rather than restricted policy on time of insertion.

In a mass IUCD program, the consideration obviously is not so much the number of insertions as the number of months of use after insertion (the retention span). Furthermore, since the major problem is scarcity of personnel, the amount of coverage by a single worker depends primarily on the number of times each woman has to be seen. A research requirement of a monthly return visit would be impracticable. Even a yearly return visit doubles the number of procedures each year. More time is needed to tell whether any return visits on a routine basis are necessary. One can imagine permitting the woman to wear the device as many years as she wishes without medical re-examination. In such a practice, what would be the annual increment of IUCD wearers at a constant insertion rate? In Pakistan, in order to have a basis for planning, an educated guess on probable retention span has been made, as follows:

Percent retained from first year of insertion	*Cumulative number in use per 100 insertions per year*
At end of 1st year 75%	75
At end of 2nd year 50%	125
At end of 3rd year 35%	160
At end of 4th year 25%	185
At end of 5th year 10%	195
At end of 6th year 0%	195

For future planning, it would be helpful to be able to estimate the probable effectiveness of an IUCD program. This might be possible for the first year, at least, on the basis of data collected during a one-year pilot project. This has been done for Pakistan, as indicated below. The calculations would not apply to the second year, since there is at present no basis for assuming unchanged effectiveness with prolonged retention of the devices. Observations of the pilot project would be necessary over a span of time equal to the period for which estimate is being made.

The data needed are the following :

Average interval between births among the women prior to their coming to the IUCD clinic. This has been determined in Pakistan to be 3 years.

Pregnancy rate that actually occurred among IUCD wearers in the project. For Pakistan, this is 1.5 per 100 woman-years of use.

Percentage of women who discontinued IUCD use. For Pakistan, this is 22 percent.

Average IUCD retention span before discontinuation. For Pakistan, this is 4.8 months.

Calculations for 100 IUCD insertions

Expected number of births without program (at rate of 33 per 100 woman-years		33.0
Estimated number of births with program (at rate of 1.5 per 100 woman-years of use)		
(*a*) Pregnancies among wearers		
1) 78% retained IUCD full year – 0.78 × 1.5	1.17	
2) 22% discontinued IUCD after average retention span of 4.8 mo. 0.22 × 4.8/12 × 1.5	0.13	
(*b*) Pregnancies after discontinuation (assuming usual rate of 33 per 100 woman-years) 0.22 × 7.2/12 × 33	4.36	5.66
Number of births prevented		27.34

In Pakistan, with approximately 5,000,000 babies born per year, a five-year effort at 20 percent reduction by means of intra-uterine contraception alone would require 1,850,000 insertions per year. Thus a quantitative basis exists for program development pointing toward an established goal.

MEDICAL EVALUATION OF THE INTRA-UTERINE DEVICES IN INDIA

by

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Studies on the intra-uterine method of conception control using a variety of materials have been reported from many parts of the world.[1-8] The use of polyethylene devices is of great value in an overpopulated country like India. The purpose of this paper is to present a report on a small clinical trial with intra-uterine contraceptive devices (IUCD) among women in India.

The Family Planning Clinic of the All-India Institute of Medical Sciences, New Delhi, introduced the IUCD as one of the methods for conception control in August, 1962. Contraindications for the use of the devices were submucous fibromyomas, adnexal disease, and pregnancy. Insertions were done irrespective of the phase of the menstrual cycle, provided the couple had taken adequate contraceptive measures prior to the insertion. Endometrial biopsies were also taken at the time of insertion. The patients were informed regarding the immediate effectiveness of the method and were instructed to return to the clinic for a check-up after their next menstrual period. Pelvic examinations were repeated at three and six months and an annual checkup was further advised. The women were requested to report immediately if the spiral or loop was expelled or if there was any other complaint.

Clinical observations

From August 1, 1962 to August 31, 1964, the IUCD has been inserted in 485 women for a total of 526 insertions and a follow-up of 2,020 patient-months. The Margulies spiral was

TABLE I

Distribution according to age

Age in Years	Number of Women
15—20	2
20—25	91
25—30	168
30—35	163
35—40	52
40—45	9
Total	485

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used for 390 insertions; the large and small sizes were used 74 and 316 times respectively. The Lippes loop was used for 136 insertions; the sizes used were 31 mm (56 insertions), 27.5 mm (62 insertions), and 25 mm (18 insertions).

Prior to the insertion of intra-uterine devices, 59.8 percent of the couples had tried other methods of contraception. More than one method was tried by many couples, including an oral contraceptive. Circumoral erosion of the cervix and trichomonal vaginitis seen at the time of the initial pelvic examination did not contraindicate the use of the IUCD.

Table I shows the distribution of age, Table II the parity, the majority of the women having from 4 to 9 children.

TABLE II

Distribution according to parity

Parity	Number of Women
1—3	87
4—6	145
7—9	157
over 9	96
Total	485

TABLE III

Duration of follow-up

Months Followed	Number of Women
0— 4	215
5— 8	87
9—12	57
13—16	15
17—20	17
21—24	2
Total	393

Table III indicates the duration of follow-up. During the first follow-up visit data collected on pain and bleeding after insertion showed that 259 women had no pain, 57 mild, 55 moderate and 13 had severe cramps and backache (Table IV). Analgesics were used when indicated.

TABLE IV

Pain following insertion

No pain	259
Mild	57
Moderate	55
Severe	13

Bleeding after insertion was classified as heavy, moderate, mild, spotting in comparison with the normal menstrual flow of the patient. Data show that 93 women had heavy bleeding, 108 moderate, 30 mild, 94 spotting, and 25 had irregular or continuous bleeding over a prolonged period of time. The remaining 25 women had no bleeding after insertion (Table V).

TABLE V

Bleeding following insertions

No bleeding	25
Spotting	94
Mild	30
Moderate	108
Heavy	93
Irregular or continuous bleeding	25

First menses following insertion can be reported in 327 women. The amount of flow was heavier in 157 and moderate or normal in 130. The IUCD was inserted during a period or bleeding after insertion merged with menses in 25. The remaining 15 had lactational amenorrhea (Table VI). Fifty-seven had menses earlier than usual, 193 on their expected date, and 11 later than anticipated.

TABLE VI

First period following insertion of device

Heavy	157
Moderate	130
Lactational amenorrhea	15
Inserted during periods	25

Data on menstrual bleeding at subsequent follow-up visits are available for 243 women. Menstrual flow was normal in 159, heavy in 71, irregular or continuous in 8, and 15 continued to have lactational amenorrhea. Menstrual periods were early in 24, at the expected time in 199, and late in 7.

Spontaneous expulsion of the device occurred 57 times in 43 women (8.9 percent). Except for one, all expulsions were known to the patient. Time of expulsion is shown in Table VII. Most expulsions occurred immediately after insertion or during the first menstrual period.

The device had to be removed from 45 women. The reasons for removal were: heavy bleeding (20), intermenstrual spotting (7), severe pain (6), dyspareunia (1), lack of enjoyment of sex (1), and psychological reasons (2). General practitioners not aware of the use of the device removed it from 3 women. One patient was leaving town and one gave no particular reason but wanted the device out. The remaining three women developed pelvic inflammation with fever and adnexal tenderness and masses.

TABLE VII

Time of expulsion

During bleeding following insertion	9
Two weeks after insertion but not during bleeding phase	1
During first period	14
During second period	8
During third period	2
During fourth period	4
During fifth period	3
During sixth period	3
During seventh period	1
During eighth period	1
Time of expulsion not given by patient	2
Expulsion unknown to patient	1
Device detected on examination lying in the cervical canal or vagina	6
Expelled after 8 and 12 months but not during a period	2
Total expulsions	57

In 2,020 months of follow-up in 485 women, 6 pregnancies occurred, giving a pregnancy rate of 3.56 per 100 years of exposure. Pregnancy resulted after unnoticed expulsion in one woman. The device was detected *in situ* radiologically in one, and in the remaining 4 pregnancies the device was undetermined. No adverse effects were noted in women with trichomonal vaginitis or circumoral erosion of the cervix.

Comments

Although the present study is of a short duration, the acceptance of the method has been satisfactory as compared to other methods tried by 59.8 percent of the couples. The study group included both literate and illiterate inhabitants of Delhi. Long-term follow-up is required for proper evaluation of the method.

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INTRA-UTERINE CONTRACEPTION IN INDIA

by

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General background

India today is involved in a desperate struggle to raise the level of living of its people through planned development within the framework of democratic government. The present low levels of per capita income, savings, and capital formation, and the high dependency load, are alarming. The excessively high rate of population growth in India now presents the most direct threat to achievement of national aspirations of economic development and social justice for all. The Indian Planning Commission has indicated that the Indian national family planning program is "at the very center of planned development."

The national family planning movement in India has the goal of reducing the birth rate to 25 per 1000 as soon as possible. For this purpose the national program is undertaking systematic efforts to:

(*a*) build community-level educational activities, aimed at helping different groups in the population to adopt a smaller family size norm, as well as to provide specific information about contraception;

(*b*) make contraceptive supplies and services of all types freely available to married couples, without psychological, physical, or financial barriers;

(*c*) strengthen statistical services in order better to understand fertility dynamics and more efficiently learn from program experiences;

(*d*) provide medical consultation services for persons who have some complications or who desire methods requiring medical handling;

(*e*) build up a strong, extensive organizational framework, in order to provide the administrative services and the continuing supervision and support required for a mass national movement;

(*f*) proceed as rapidly as possible with activities in the fields of training, supply, and research, as needed for implementation of the above program; and

(*g*) encourage further liberalization of social policies and legislation which may help to accelerate changes in fertility behavior; suggestions to be considered include raising the legal age of marriage, and encouraging women to enter the labor force through better education and employment opportunities[1]. A committee is also being appointed to review the abortion laws.

It is abundantly clear that the process of fertility change is a complex and multi-factorial affair. The acceleration of this process calls for application of maximum imagination and effort at every possible point in the system. Among the very important factors in the program, of course, is the availability of contraceptive methods that are cheap, effective, and acceptable to the people. However, it should be stressed here that it is at least naive, and it can be dangerous, to expect that improvements in contraceptive technology alone can do the whole job, without concomitant attention to other aspects of the total system.

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Also, it must be emphasized that no one contraceptive method will meet the needs of all the people. Individuals are different, and are inclined towards different kinds of methods. One couple may use several different kinds over a period of time. In India, the use of surgical sterilization has in some areas become a popular movement. The voluntary sterilization program is growing to important proportions. There is also a steep rise in the use of condoms. Use of non-mechanical methods is widespread and probably increasing rapidly. All present methods which the people find useful and acceptable should be made even more widely available in order to catalyze the total process of change.

There is no doubt, however, that further improvements in contraceptive technology can greatly help to accelerate the process of demographic transition. Any such advances should be added to the contraceptive armamentarium as rapidly as possible. For this reason, the prospect that intra-uterine contraceptive devices are now suitable for more widespread utilization is very heartening. This method, which has the advantages of a "one-time" action of insertion, high effectiveness, and easy reversibility, will certainly be attractive to a large section of the population.

Earlier experiences in India

Ancient Indian medical writings dealt extensively with contraception and contraceptive methods, but did not apparently include the specific idea of intra-uterine contraception. Abortion was well known in indigenous medical lore, but the concept of *preventing* the fertilization process through mechanical means in the uterine cavity was not mentioned.

The work of Gräfenberg in the 1920's aroused interest in India, and a number of medical people began to use the silver ring. In Ahmedabad, the late Dr. (Miss) C. Baptista had a series of over 2,000 cases with this method. Dr. S.B. Anklesaria pointed out the advantages of intra-uterine contraception to the Ahmedabad Obstetrical and Gynecological Society as early as 1938. Dr. Anklesaria reported on 319 cases in 1962.[2] Still, Indian workers have been troubled with the complications attending the use of silver devices, as have workers in other countries. Dr. M.D. Saigal in Gujerat reported on 13 persons having such problems.[3]

The favorable reports of Oppenheimer and of Ishihama in 1959 helped to stimulate further interest in India. In 1960, Dr. (Mrs.) A. Dass, of Delhi, undertook a study of the use of silkworm gut devices.

In the meantime, the further development of plastic materials which do not cause foreign-body reactions in human tissues was making possible remarkable advances in the field of reconstructive surgery, and pointed the way towards use of these materials for further improvement of intra-uterine contraceptive devices. Samples of experimental plastic devices were kindly sent to us by Dr. Margulies of New York. Dr. Shirodkar in Bombay undertook studies of such devices, being especially concerned with possibilities of detecting the device through magnetic means. Dr. Purandere, at the K.E.M. Hospital in Bombay, also started some studies.

In 1962, the International Conference on Intra-Uterine Contraception, held in New York, was attended by Dr. Shirodkar on behalf of the Government of India. The excellent results reported at this conference, covering over 6,500 patients during nearly 10,000 woman-years of experience, helped to bring Indian researchers into closer contact with the extensive experience being accumulated elsewhere. Further assistance in this field was provided by Dr. Sheldon J. Segal and Dr. Anna Southam, who were in India under the auspices of the Ford Foundation.

Recent developments

In 1962, the Ministry of Health requested the Indian Council of Medical Research to examine the whole area of intra-uterine contraception. A special committee was formed for this purpose and a review report was prepared for the use of Indian investigators.[4] The Committee recommended that the Director of the Indian Council of Medical Research should invite proposals for further carefully developed studies on the use of IUCD in India. This recommendation was endorsed by the Government of India, and an *ad hoc* committee of the Indian Council of Medical Research has continued to provide guidance to these studies in India. The Committee has had very valuable help from Dr. Katherine Kuder, Consultant in Family Planning with the Ford Foundation.

Basic criteria were laid down for the establishment of such studies, and a standard guide for investigators and a detailed standard record form were developed. The Population Council kindly offered 8,000 plastic devices, including spirals and four sizes of loops, with inserters. These have been provided to qualified investigators.

The inquiries now under way are of two general types:

(*a*) studies primarily concerned with mechanism of action of the devices, and

(*b*) clinical trials which are primarily concerned with assessment of acceptability and with the detection and clarification of any possible problems to be encountered during large-scale use of the devices at a later date.

Important studies on the mechanism of action are under way in the All-India Institute of Medical Sciences in New Delhi.[5,6] Dr. P. Malkani introduced intra-uterine devices into a group of rhesus monkeys by abdominal hysterotomy in 1962; these animals are still under observation, to detect any possible long-term effects on pelvic organs. Notable observations have been made by Dr. Sujan. Dr. A. Farooq has been studying the effect on implantation of introducing a suture in one horn of the uterus of rodents; this is linked to a broader study of the response of uterine endometrium to gonadal hormones. In this Institute, clinical studies of the effects of IUCD are also being correlated with histological, biochemical, and bacteriological examinations. Dr. Malkani and her colleagues have studied sperm migration in the female reproductive tract in the presence of intra-uterine devices.

At the Central Drug Research Institute in Lucknow, Dr. A.B. Kar has also investigated the mechanism of contraceptive action of IUCD, using rats, rabbits, and monkeys. His paper, entitled "*Experimental Studies on Intra-uterine Contraception*", is being published in the *Proceedings* of this conference.

At the Institute of Agriculture, Anand, in Gujerat, Dr. N.C. Buch has been studying the mechanism of intra-uterine devices in goats and cows. He has recently presented a paper at the Fifth International Conference on Animal Reproduction and Artificial Insemination, on the effect of the devices in Indian water buffaloes.

Clinical trials carried out under the Indian Council of Medical Research program first began in August 1962. These trials are now being conducted in 48 different urban and rural locations in India, so that all varieties of cultural groups, levels of literacy, and economic and social conditions are represented among the women under study. The trials are being carried out by the departments of obstetrics and gynecology and the family planning clinics of 16 medical colleges, 11 maternity or general hospitals, 7 family planning association clinics, 5 family planning training centers or reproduction research units, 4 mission hospitals, 3 municipal clinics, and 2 public transportation health units.

Sixteen studies began before December, 1963, and the remaining 32 since then. Over 2,000 women are under observation. Data are now being analyzed and a full report will be available by the end of 1964. However, it is possible now to provide some general impressions from the experience gained.

Over-all acceptance of this method has been excellent. News of this method of contraception has spread widely by word of mouth, and women have come from long distances to request it. It is felt that an even greater demand will be created when this service is tied with educational activities and brought closer to the place where the people live.

So far, the incidence of problems or complications has appeared to be on about the same small scale as reported from studies in other parts of the world. It is notable that even though a small percentage of women do have some discomfort with the IUCD, many of these still refuse to have it removed. The loop type appears to have fewer spontaneous expulsions than the spiral. Infection has not been a significant problem. Health authorities and medical practitioners are increasingly expressing eagerness for a wider availability of the method.

Further steps

It is hoped that an Indian conference on intra-uterine contraception may be convened before the end of 1964, in order to pool the data and experience of researchers all over India on this subject. The discussions from the Second International Conference on Intra-Uterine Contraception will further enrich this meeting. The Indian conference should provide a solid basis for inclusion of intra-uterine contraception within the national family planning movement. The extension of this aspect of the program will involve further development of certain aspects of procedure, supply, and organization.

Procedural aspects. It is felt that the clinical experience now in hand can provide a sound basis for detailing standard procedures and policies which will be suitable for use on a more extended scale. For example, in India where the incidence of cervical erosion and low-grade infection may be relatively high, some standard guidelines for handling such cases will be needed.

Some simplified guidelines regarding possible contraindications to insertion may also be evolved. It has been suggested in the past that women with fibroids or carcinoma should be excluded. This question may be generally rather hypothetical, in that women with such conditions would be less likely to seek contraceptive help; even if they did, the insertion of the IUCD, of itself, may not be dangerous.

Since a number of those who receive devices have noticable bleeding during the first month or so, and women in India may tend to have a low hemoglobin, it has been suggested that at the time of insertion women might routinely be given a week's supply of iron and, perhaps, multivitamin tablets. The value of such a procedure could be assessed. This again, however, would be the type of more refined question which can be studied in the course of an extended service program. It will help to know the mode of action of IUCD and to develop them to reduce the incidence of removals and expulsions.

Supply problems. Exploratory discussions are now under way for the manufacture of devices in India, to meet the needs of current studies and of further extension of services.

There is need also to produce better inserters, so that under adverse conditions they do not become brittle or misshapen. Since the plastic inserters cannot be boiled, there is need to identify cheap, stable, antiseptic solutions, which do not harm the inserters and are suitable for routine use in rural areas.

Not the least of the production challenges is the possibility of developing a universal type of device and inserter which might reduce the need for stocking different sizes. Both the design and material should be made as simple as possible. For example, it seems unnecessary to add barium to the loops meant for use in an extended program where there may only rarely be need for X-ray location of the device. Also, the small attached thread need not be dyed. Further consideration should also be given to the development of simple devices made wholly of material like nylon thread, although some have questioned this on account of the moisture-absorbing property of nylon.

Organizational aspects. Preliminary plans are now being laid at the Central Family Planning Institute, in New Delhi, regarding the training strategy required for including the use of intra-uterine contraception in the extended family planning program in India. This will require a series of short seminars for medical leaders and others from the states of India. They, in turn, can utilize their institutions and the state family planning training centers to provide a systematic orientation program for the medical personnel in their own states.

No difficulty is anticipated in training medical graduates to insert devices. Establishment of IUCD clinics within present health facilities may make this method easily available in urban situations and in those villages where maternal and child health clinics have been established. Special emphasis will be needed, in these situations, to reduce record-keeping strictly to the bare minimum, and to simplify procedures so that women need not wait unnecessarily or encounter other psychological barriers to acceptance.

However, such hospital facilities or child and maternal health services still do not reach an appreciable part of the population. How can the method be truly made widely available? One very practical approach to this problem in India has been the use of mobile "camps." In these, a well qualified surgical team sets up temporarily in a rural location; through prior arrangements large numbers of rural people can assemble there to take advantage of the service offered. For many years, this method has worked well for the performance of cataract operations on a mass scale. In recent years, it has also had remarkable success in meeting the demands for voluntary sterilization operations. For example, in 1963 at Satara in Maharashtra State over 1,000 vasectomy operations were performed at a single camp. In Gujerat State the same camp technique has been used for female sterilizations. In Gujerat State, also, the camp technique has been tested for its applicability to insertion of intra-uterine devices and has been found satisfactory.

It is noteworthy that the process of arranging for such camps takes special effort, and in itself has a considerable group-educational effect. Also, the people who come to the camps seem to derive additional psychological support from each other. The organizational pattern now being developed by the Indian family planning program should be ideally suited for arrangement of such camps on a regular basis.

Summary

Indian researchers have long had an interest in intra-uterine contraception, and this interest has spread rapidly during the past few years. Under the leadership of the Indian Council of Medical Research, over 50 institutions throughout the country are now involved in (a) studies on the mechanism of action of IUCD, and (b) clinical trials to clarify any medical problems which might arise during mass use of such a method in India. So far, it has appeared that the method is highly acceptable and that complications are minimal. Some details of use, procedure, and policy still need clarification and standardization. Help is needed, also, in solving problems of production. It is anticipated that data from current studies in India can soon be brought together and can provide the basis for expanding the use of this method as part of the national movement. After an extensive but brief training program, the method could be made available initially through existing clinical facilities. The "camp" approach, as already used effectively in India for eye operations and sterilization operations, may be especially applicable to the more widespread promotion of intra-uterine contraception.

All evidence now indicates that improved intra-uterine contraceptive methods will be an exceedingly important addition to our contraceptive armamentarium. But let us also remember, at this exciting moment, that the promotion of a mass family planning movement for a whole nation is a complex matter, which requires that effort and attention be given to many different factors. We must avoid the trap of pinning excessive hopes only upon the more tangible and familiar subject of improved contraceptive technology. In countries where communication systems and social services are not highly developed we must still provide for sound, continuous, imaginative family planning educational activities. And we must still build up the firm and extensive organizational base which is required in order to apply effectively what we know.

ACKNOWLEDGEMENT

The Population Council has been exceedingly helpful, in generously supplying intra-uterine devices, in arranging this Conference and extending invitations to workers from India, and in other ways; this assistance is deeply appreciated.

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THE INTRA-UTERINE DEVICE PROGRAM IN KOREA

by

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Evaluation of the safety and effectiveness of intra-uterine contraceptive devices (Lippes loops) in Korea was originally initiated in Seoul by the Planned Parenthood Federation of Korea (P.P.F.K.) in 1962. Two medical school hospitals and a missionary mobile clinic were selected as participating clinics.

The government, deeply interested in the intra-uterine contraceptive device as a method of controlling the rate of population increase, decided to support and extend the evaluation study in December 1963. IUCD clinics in 21 medical school and provincial hospitals throughout the nation were established, and 24 obstetricians and gynecologists were trained. The extended study has been under way since January 1, 1964 under the supervision of the Medical Advisory Committee of the P.P.F.K. The government provides loops and inserters, and pays a subsidy for each insertion and two years' follow-up. Responsibility for the collection and processing of data and for their analysis was assigned to the Department of Obstetrics and Gynecology, Seoul National University Medical College. Figure 1 shows the locations of original and extended evaluation clinics.

In April 1964, following the intermediate report derived from the original evaluation study for 16 months of observation up to March 1, 1964, which indicated a high degree of effectiveness and acceptability, the government decided to introduce the loop on a voluntary nationwide basis, with the cooperation of the Medical Advisory Committee of the P.P.F.K.

In order to provide the high level of service essential to public acceptance on a national scale, 120 volunteer Ob-Gyn specialists practicing in all parts of the country were given training and their clinics were designated as paying IUCD clinics where loops would be inserted for clients desiring to try this new method of contraception. The government is supplying loops and inserters, and clients pay the doctors for insertion of the devices.

After one month's trial of this approach (May 1964), results were so encouraging that it was decided to include loop insertion as a regular part of the national family planning program. Preparation for adding the loop to the regular program involved the training of 301 general practitioners, providing them with loops and inserters, and designating their clinics as free IUCD clinics for referrals by local family planning workers at health centers. These 301 free clinics have been open since June 1, 1964. Referrals to free clinics are limited to patients unable to pay for the insertion. The government is paying a subsidy for each insertion and 6 months' follow-up, and supplying loops and inserters through the health centers.

The health centers, which execute the administration of projects in the field of public health, are the focal points for governmental family planning activities. There are 189 health

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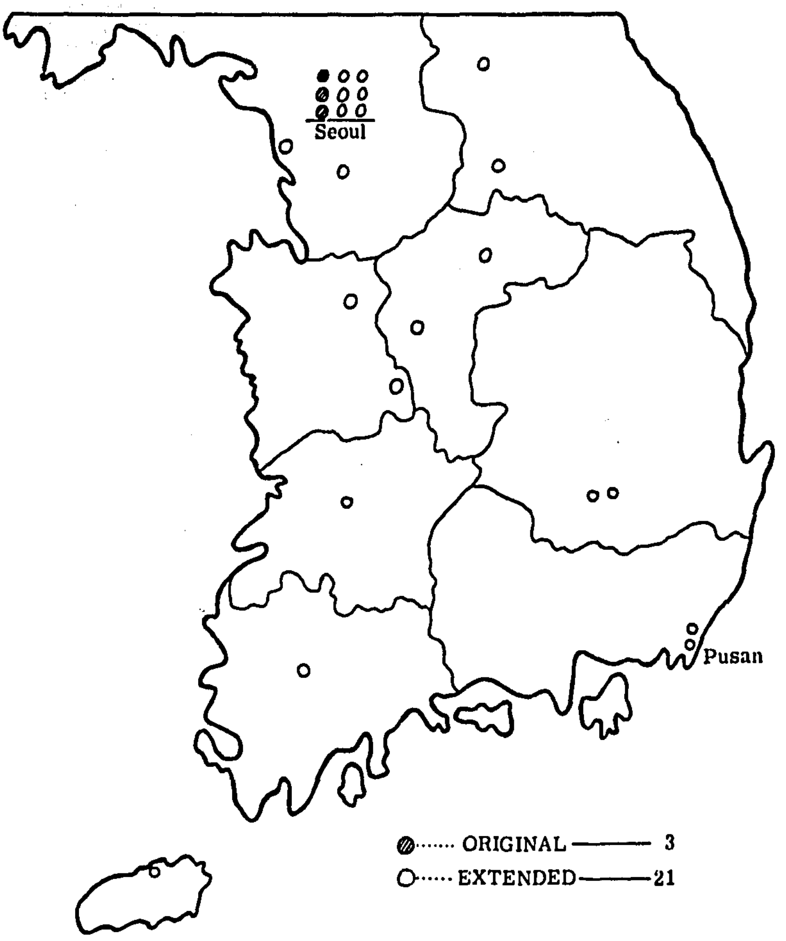

Fig. 1. Locations of original and extended evaluation clinics.

centers distributed throughout Korea, each serving an average population of 150,000. Each health center has three or four family planning field workers, who are qualified nurses or midwives. In addition, every township, containing an average population of 10,000, has one assistant field worker who is a qualified nurse or high school graduate.

Field workers of each health center issue coupons to clients who want the IUCD. The client takes her coupon to a free clinic, where a doctor makes the insertion if his examination reveals no contraindications. The subsidy for insertions is paid at the end of each month through the health center in exchange for returned coupons, and each health center reports the number of insertions to the central government monthly. A woman who has been fitted with the loop carries a registration card, issued by government, on which the date of her next visit and instructions after insertion are shown. Field workers of the health center and townships are instructed to help follow-up by home visits.

Both paying and free IUCD clinics are supplied with simple recording cards, and they are asked to send copies to the central government after the completion of six months of follow-up. The first results and analysis of the data from these clinics will not be available until after January 1965.

The government's original goal of insertions with free service was 70,000 for 1964, but the target has been raised to 100,000. As of July 31, 1964, a total of 445 clinics were participating in IUCD service: 24 clinics for evaluation study, 120 paying clinics, and 301 free clinics. The government trained 418 additional general practitioners in September 1964, and the number of free IUCD clinics will be increased to 719.

The total number of insertions as of July 31, 1964 was 38,350. The monthly breakdown is shown in Table I.

TABLE I

IUCD Insertions up to August 1964, by month

Type of Clinic	No. of Clinics	Number of Insertions								
			1964							
		Up to 1964	Jan.	Feb.	March	April	May	June	July	Total
Evaluation	24	1,493	1,527	1,524	1,949	871	1,612	1,412	638	11,026
Paying	120						1,773	697	446	2,916
Free	301							13,571	10,837	24,408
Total	445	1,493	1,527	1.524	1,949	871	3,385	15,680	11,921	38,350

TABLE II

Insertions at 3 evaluation clinics, by age and parity

Age	Total
20–24	59
25–29	711
30–34	1,578
35–39	1,310
Total	3,658

Parity	Total
0	6
1	67
2	332
3	816
4	935
5	773
6	420
7	193
8	84
9	26
10 or more	6
Total	3,658

Analysis of original evaluation study

Materials and method: The devices used in the original evaluation study at three clinics were Lippes loops, size 1 (24 mm.), size 2 (31 mm.) and size 4 (27.5 mm.). Residence nearby, availability for easy follow-up, age under 39, and parity of one child or more, were set up as criteria for admission. History and pelvic examinations were carefully done and patients with contraindications (fibroids, acute and subacute pelvic inflammatory disease, carcinoma and suspicion of carcinoma, or a history of recent metrorrhagia or menorrhagia) were excluded from the study. The distribution of patients by age and parity is shown in Table II.

The insertions were made immediately after the end of menstruation, to avoid the possibility of pregnancy before insertion. Patients were given advice on the possibility of cramps and bleeding after insertion, increased flow in the first and second menstrual period, and spontaneous expulsion. Patients were also instructed to return for follow-up every month for three months, then every three months for three visits, and two more visits with six-month intervals. If they did not return, they were contacted by telephone or mail, or visited by the public health nurses.

TABLE III

Discontinued cases: pregnancies, expulsions, and major relevant removals, by months of use

	Months of Use																		
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	Total
	Loop size 1																		
Pregnancies																			
In situ	0	0	3	4	10	3	4	4	4	1	0	1	2	1	1	1	0	0	39
Expulsions	0	0	0	4	2	0	1	2	0	1	0	0	1	0	0	0	0	0	11
Expulsions																			
Noticed	9	16	13	3	5	1	4	1	1	3	1	1	1	2	1	0	0	0	62
Unnoticed	3	8	5	4	3	3	1	0	0	0	2	0	0	0	0	0	1	0	30
Removals																			
Bleeding	7	14	1	4	2	3	0	0	0	1	1	0	0	0	0	0	0	0	33
Pain	8	9	11	6	2	2	1	2	7	3	1	0	2	1	2	0	2	0	59
Leukorrhea	0	2	0	0	1	1	0	0	0	0	0	1	2	0	0	0	1	0	8
Infection	0	2	0	0	2	3	1	0	0	0	0	0	0	0	0	0	0	0	8
Fear	3	10	1	4	1	2	2	0	2	1	1	1	1	0	0	0	0	0	29
Total	30	61	34	29	28	18	14	9	14	10	6	4	9	4	4	1	4	0	279
	Loop size 4																		
Pregnancies																			
In situ	0	1	0	1	1	0	0	0											3
Expulsions				1	1	0	0	0											2
Expulsions																			
Noticed	7	16	10	2	7	0	0	0											42
Unnoticed	0	2	2	0	0	0	0	0											4
Removals																			
Bleeding	10	15	5	0	2	0	0	0											32
Pain	18	20	7	9	6	2	0	0											62
Infection	0	1	0	0	1	0	0	0											2
Fear	6	1	2	4	2	3	1	1											20
Total	41	56	26	17	20	5	1	1											167

Months of exposure: As of July 31, 1964, a total of 3,658 women had been fitted with the Lippes loop at the three original evaluation clinics. Among them, 1,834 women were fitted with size 1, 1,595 with size 4 and 229 with size 2. A total of 9,662 months of exposure has been accumulated with size 1, 2,600 months of exposure with size 4, and 118 months of exposure with size 2. No conclusions were drawn for size 2, in view of the short period of observation to date.

Discontinued cases: A total of 436 women (23.8%) wearing size 1, and 176 (11.0%) wearing size 4 have been discharged from the study for both relevant and non-relevant reasons.

Pregnancy occurred after insertion in 50 out of 1,834 size 1 wearers (2.7%), and 5 out of 1,595 size 4 wearers (0.3%). Eleven of 50 pregnancies in size 1 wearers and 2 of 5 pregnancies in size 4 wearers occurred following unnoticed expulsion. Pregnancy rates per 100 woman-years of exposure were 6.2 for size 1, and 2.3 for size 4.

Ninety-two (5.0%) size 1 wearers and 46 (2.9%) size 4 wearers expelled the device spontaneously. Thirty of the 92 expulsions in size 1 wearers and 4 of the 46 expulsions in size 4 wearers were not noticed by patients.

Loops were removed for relevant and non-relevant reasons from 211 (11.5%) size 1 wearers and 123 (7.7%) size 4 wearers. The reasons for relevant removal range from medical necessity to the personal preference of the couple.

The major reasons for relevant removal of sizes 1 and 4 were pain and bleeding, as shown in Table III. Pain required removal of the device from 59 (3.2%) women wearing size 1 and 62 (3.9%) women wearing size 4. Bleeding led to removal from 33 size 1 wearers (1.8%) and 32 size 4 wearers (2.0%).

TABLE IV

Analysis of original evaluation study

	Loop 1	Loop 4
Total insertions	1,834	1,595
Total carrying to date	1,398	1,419
Total discontinued	436	176
Total months of exposure	9,662	2,600
Analysis of discontinued cases:		
Total insertions	1,834	1,595
Total discontinued	436 (23.8%)	176 (11.0%)
Pregnancies	50 (2.7%)	5 (0.3%)
Device *in situ*	39	3
Device expelled	11	2
Pregnancy rate (per 100 woman-yrs)	6.2	2.3
Expulsions	92 (5.0%)	46 (2.9%)
Noticed	62	42
Unnoticed	30	4
Removals	211 (11.5%)	123 (7.7%)
Relevant removals	144 (7.8%)	114 (7.1%)
Non-relevant removals	67 (3.7%)	9 (0.6%)
Moved away	8 (0.4%)	0
Not contacted	75 (4.1%)	0

Size 1 loops were removed from 8 wearers who developed leukorrhea. Twenty-nine size 1 wearers and 20 size 4 wearers requested loops to be removed because of fear and anxiety.

One patient wearing size 1 underwent radical hysterectomy following a diagnosis of carcinoma of the uterine cervix by biopsy after 14 months of use.

Seventy-five size 1 wearers were lost to follow-up for more than 12 months and eight moved away; these were discharged from the study. Table IV presents an analysis of the original evaluation study.

If the unintended pregnancies, expulsions, and relevant removals are categorized as relevant reasons for discontinuation which bear on the effectiveness and acceptability of the devices, 286 women wearing size 1 (15.6%) and 165 women wearing size 4 (10.3%) discontinued the method or were discharged from the study due to relevant reasons.

Analysis of extended evaluation study

The Lippes loop size 4 was used in the 21 extended evaluation clinics. Criteria for admission, schedule for follow-up, and record-keeping were the same as in the original study.

A total of 5,582 cases was available for analysis from this extended study, and a total of 10,055 months of exposure had been accumulated as of July 31, 1964.

As shown in Table V, the pregnancy rate was 2.6 per 100 woman-years of exposure and the rates of expulsion and removal were 2.9 and 9.6 percent respectively.

TABLE V

Comparison of original and extended study, using Lippes loop 4

	Original	Extended
Total insertions	1,595	5,582
Total carrying to date	1,419	4,852
Total discontinued	176	730
Total months of exposure	2,600	10,055
Analysis of discontinued cases:		
Total insertions	1,595	5,582
Total discontinued	176 (11.0%)	730 (13.1%)
Pregnancies	5 (0.3%)	22 (0.4%)
Device *in situ*	3	17
Device expelled	2	5
Pregnancy rate (per 100 woman-years)	2.3	2.6
Expulsions	46 (2.9%)	166 (2.9%)
Noticed	42	92
Unnoticed	4	74
Removals	123 (7.7%)	537 (9.6%)
Relevant removals	114 (7.1%)	508 (9.1%)
Non-relevant removals	9 (0.6%)	29 (0.5%)
Moved away	0	5 (0.1%)

Conclusions

In the original evaluation study, the pregnancy rate for size 1 wearers was 6.2 per 100 woman-years of exposure, which is higher than the rate of 2.3 for size 4 wearers. Two-thirds of the pregnancies occurred during the first 6 months of use.

The expulsion rate was 5.0 percent in size 1 wearers, but only 2.9 percent in size 4 wearers. Most expulsions occurred within 3 months of insertion.

The major reasons for relevant removal were pain and bleeding. The incidence of pain and bleeding requiring removal is greater in size 4 wearers than size 1 wearers.

These findings indicate that size 4, a larger size, is more effective than size 1 in the prevention of unintended pregnancy, and is expelled less frequently, but side effects requiring removal, such as bleeding and pain, are more frequent with size 4.

Comparison of the results from the original evaluation study and those of the extended evaluation study will be of value as the first step of the national IUCD program. As shown in Table V, there is no significant difference between the two evaluation groups.

The results indicate that the Lippes loop provides a safe, reliable, and acceptable means of contraception in Korea.

In this study, only two sizes of the Lippes loop, size 1 and size 4, were evaluated. The largest size of Lippes loop, size 2, which is supposed to give better results, is being evaluated. However, I believe that there should not be a single standard size for a nation but that the best size for the individual patient should be selected from a range of available sizes.

THE USE OF AN ITINERANT PHYSICIAN TO INTRODUCE THE INTRA-UTERINE CONTRACEPTIVE DEVICE IN MEDICALLY DISADVANTAGED AREAS

by

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The intra-uterine method of contraception requires convenient and inexpensive clinical services, whether public or private, or one may lose the advantages of convenience and inexpensiveness that are so nicely inherent in the device itself. There is some reluctance on the part of certain workers in population control to accept the clinical approach as an effective method of population control. They point to India as an example, and that country's disappointment with its early clinical services. India's Family Planning Annual Report (1962-63)[10] states that "the *clinic approach* could be expected to reach only a relatively small fraction of the people, and could not be expected to make much impact on birth rates." Before and during the time that India tried to introduce the vaginal methods of birth control through clinics it is estimated that the Japanese were manufacturing at least 100,000 intra-uterine devices a year.[13] These devices, the Ota ring and the rubber-covered metal "Y" type, were generally well accepted by women who were the patients of certain private physicians in Japan, Korea, and Taiwan. This helped prepare the way in Asia for the intra-uterine method. By early 1963, field studies were under way in several countries, including Korea, Taiwan, and Pakistan, to confirm, if possible, the favorable reports of safety and effectiveness which were given at the first conference on intra-uterine contraceptive devices on April 30 and May 1, 1962.[15]

These three Asian countries were not only testing the biologic effects of the device but were also studying ways of providing convenient and inexpensive clinical services to all women regardless of economic status. It was discovered independently by these three countries that one itinerant woman physician could travel between properly spaced simple clinics more easily than one could expect many women to travel to a central clinic. These itinerant physicians were relatively successful in introducing a birth control program through a clinic approach because it provided easy accessibility to an easily practiced method of contraception. There are advantages for poor and busy mothers in this program as compared to a program that seeks to motivate women to walk an hour or take a bus to an official health center, where after answering some questions she can receive a dozen condoms or a vial of foam tablets or even a diaphram.

To begin with, Taiwan and the Republic of Korea have similar social, cultural, and racial characteristics.[2,3] Demographic characteristics are also similar, with the major exception that Taiwan, with a population of 12 million, has slightly less than half the total population of South Korea. Surveys in both countries have shown that over 80 percent of the married women approved of birth control, but that fewer than a quarter of them employed any

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means of contraception. The women were in general poorly informed about family planning methods and their use in many cases was without success. They expressed strong interest in learning and adopting better methods of birth control.

The Taiwan program was begun in the city of Taichung, which has a population of about 300,000.[14] The program included the entire city, which in turn drew women from the surrounding rural areas. The Taiwan program included some women with more education and higher income than the smaller programs in Korea and Pakistan that will be discussed later.

It is interesting that in Taichung one woman physician did two-thirds of the 6,048 insertions of intra-uterine devices. She was able to do this by travelling between the nine health stations scattered throughout Taichung. She conducted half-day clinics in each, usually one a week. It has been stated that her diligence and enthusiasm contributed a great deal to the success of the program.

There was also a central Maternal and Child Health Institute clinic which was staffed by physicians from the medical schools. This clinic operated six full days a week and one evening a week. In a city as large as Taichung it is advantageous to have at least one central clinic which is open every day for insertions and also available for the occasional complications that will occur when a large number of women are using the device.

Those involved in the study believe that the impact on the birth rate of Taichung is likely to be considerable. They also state, "There is little doubt that the success of the program, with word-of-mouth communication playing such a prominent role, depended on the availability of the intra-uterine device."[14]

In Pakistan, the Medical Social Research Project (MESOREP) at Lulliani has offered the intra-uterine method and vaginal methods of contraception since November, 1962.[4,12] Lulliani is a town of approximately 12,500 and is considered rural. There is about 15 percent literacy and considerable social and economic stress.

In March 1964 MESOREP, in cooperation with the national study of intra-uterine devices, extended services to two nearby rural dispensaries. This was done through a mobile team which included one medical research officer (female), two female family planning workers and a driver-interpreter who also did clerical work and helped with sterilization of instruments. The dispensary has a physician and a nurse or midwife regularly stationed there. There has been some unfavorable reaction to the bleeding experienced by women attending these clinics and the removal rate has been twice as high as in Lulliani during the first 15 months of the program. However, they may find (as they did in Taiwan, Korea, and also in Michigan) that the removal rate drops as the staff gains experience in selection of patients, techniques of insertion, and choice of device, and in the management of post-insertion and excessive menstrual bleeding. As of June 30, 1964, there had been 69 insertions during four months in the two rural dispensaries as compared to 326 in Lulliani during 20 months. Thus, it is too early to evaluate the work of their mobile team.

When one is considering how to introduce a program of birth control it is, of course, necessary to know as much as possible about the country and its people. As one considers the Republic of Korea, some of the significant facts are that it has a population of about 27 million people, with a density of 270 persons per sq. km.[5] Eighty percent of the land is mountainous, and it is easy to see that as the population rapidly expands, the 70 percent of the population that is rural seeks to move from their tiny farms (average two acres) into the cities, and especially into Seoul. For various reasons the population of Seoul has increased by at least one million in the last decade. The birth rate of the entire country exceeds 40 per thousand and the death rate is about 11 per thousand. Thus they have an annual population increase of 3 percent. The *per capita* income is seventy dollars per year.[16] The economy is burdened with the support of the fourth largest army in the world and simply cannot provide, for example, the education (over 80 to a classroom, two shifts a day) and medical care which the 40 percent of the population under age fifteen require. This mass of juveniles and the 20 percent unemployed or under-employed males cannot contribute to the economy. The Korean government is mobilizing what resources it can to control population growth. Practically all of their annual budget of one million dollars for maternal and child health is designated for family planning.[1] It is probably the first country to make a nation-wide effort to use the intra-uterine method of contraception. Until more local funds or foreign aid for birth control are available they must make efficient use of the scarce economic resources now available. The intra-uterine device itself is inexpensive. The inserters, however, are somewhat more expensive and it is felt that an excessive number is often requested. But it is the program itself which is proving to be expensive.

During the past year the government provided a subsidy for those who cannot afford to pay, of $2.25 per insertion, to 420 private physicians and 24 hospitals or clinics throughout the country. The government also provided the devices (Lippes loop B)* and inserters, which are now being manufactured in Korea. The intra-uterine method is popular in the cities, so that the budget for three months is frequently depleted in one month. There certainly are not sufficient funds to expand the subsidy program to rural areas, nor to the really medically disadvantaged areas of the cities.[9]

Another problem has been the difficulty in obtaining benzalkonium chloride (*Zephiran*), which must be imported. The 24-hour immersion time suggested for chemical sterilization in *Zephiran* aggravates the shortage of inserters. It became apparent that an inexpensive, locally made chemical which could provide rapid and safe sterilization under a variety of conditions was needed.

In September, 1962 an attempt was made by a voluntary agency to solve these problems.[8] The agency introduced a mobile team to provide safe, inexpensive, easily available intra-uterine contraception services to women in four medically disadvantaged areas of Seoul and one government health center located 25 miles from Seoul at a rural village called Sosa. The study includes the first 1,400 women who received the intra-uterine device, but this report includes only the 1,035 women who have had at least 12 months' experience. These women were on the average 34 years old, had borne 5 children and had miscarried once in 14 years of married life. Allowing 10 months for each birth and 4 months for each abortion, the pregnancy rate was 60 per 100 couples for each year of exposure to pregnancy. The approximate average family income was 2,000 won, or $8.00 a month.

It was found that an itinerant woman physician who had previous gynecologic experience, assisted by an alert clerk and a good nurse, could on a very busy day do 65 insertions of loop A. In order to make a large number of insertions possible and have the service satisfactory to the patient and the staff it was necessary to have considerable contact with the women prior to and following the day of insertion. Since the clinics were conducted in the nurse's home or in a building very near her home, she provided the necessary continuous, convenient contact with the women, who generally lived in the extremely crowded neighborhood of the clinic.

The nurses also had a good reputation because for several months they had provided milk for hungry infants, immunizations for hundreds of children, and treatment for many of the

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* Designations of Lippes loops are as follows:

Size mm	No.	Letter
31	2	D
30	3	C
27.5	4	B
25	1	A

sick through another itinerant physician who visited the clinics each week. Family planning education and some service had been integrated into this medical program. However, prior to the introduction of the intra-uterine method there was minimal acceptance of rhythm, vaginal methods, withdrawal, and vasectomy. On the other hand, there was immediate good acceptance of the intra-uterine method. A new twenty-five cent charge for insertion failed to discourage the women. This fortunate high acceptability decreased the importance of intricate schemes to motivate women to accept and use contraception.

After the introduction of the intra-uterine method, the nurses' attitudes changed. They became optimistic and hopeful about family planning and enthusiastically taught women about the new method as they came for food, immunization, or medical care. They used teaching aids such as pelvic models and diagrams to explain where and how the device would be inserted. They carefully scheduled those who requested insertion so that the physician did not have to wait for patients and could use her time effectively and efficiently. The clerk took notes from the physician as she worked with the patient. This, of course, saved valuable time for the physician and enabled her to use all her time in direct contact with the women. After the physician left the clinic the nurses handled initial complications such as bleeding, cramping, expulsions, and anxiety. The women were carefully instructed to contact the nurse if they had any problems following insertion, and to return for the physician's follow-up examinations (at 5 weeks, 3 months, 6 months, then yearly). The nurses gave aspirin for cramping. They usually suggested rest and an ice bag over the pelvic area for bleeding. Occasionally they gave oral vitamin K for bleeding. If the bleeding seemed excessive the nurses occasionally would remove the intra-uterine device. Most women, however, could safely wait for the weekly clinic to see the doctor. In cases of infection or persistent bleeding, even after removal, the nurse referred the patient to the physician, who had a private hospital in Seoul. The physician was available in the evenings at the hospital. She also performed twelve dilatation and curettage operations on nine women who became pregnant following unnoticed expulsions and on three women who became pregnant with the device in place.

After a time the number of women coming to the special birth control clinic decreased. Dr. Peter Boelens, who directs this program in Korea, reorganized the program to include both medical treatment and birth control services at the same clinic. Women who desire both services are given preferential treatment and are seen first in the medical clinic. Such flexibility in programming has resulted in adequate numbers of women coming for insertion and follow-up.

Once every two weeks the physician and clerk visited the health center at Sosa and conducted a clinic. This too was an effective way to use a physician in a rural area. Two full-time family planning nurses provide the continuous contact with the rural women. The busy full-time health center physician provided occasional help on problems that the nurses could not manage.

To evaluate the program after twelve months' experience by 1,035 women in or near Seoul: There were 84 percent who had two or more follow-up examinations. There was a 7 percent expulsion rate for the Lippes loop A, which was used exclusively in this study. Half of the women noticed the expulsion and half of the women who had expulsions had re-insertions. Eighteen percent were removed: 6 percent for reasons related to the device, predominantly bleeding and pain. There was a total of 686 years of experience, and the pregnancy rate was 2 per 100 woman-years of experience. There were seven cases of infection: four from contact with gonorrhea following insertion; two from previous pelvic inflammatory disease; and one apparently from cervicitis accompanied by a heavy discharge prior to insertion. Approximately 50 percent of the women had cervicitis at the time of insertion. It would be difficult to refuse all women with cervicitis and the one infection does not seem to justify such refusal.

This intra-uterine birth control program is economically practical if the physician is kept busy. The individual subsidy, on the other hand, becomes increasingly expensive for the government in the same situation. There is also no need to hire a full-time family planning physician for each urban clinic or rural health center unless demand is very high. When the birth control program is integrated with treatment and other preventive programs it not only increases acceptability but reduces the need to hire as many additional nursing, educational, and clerical personnel as a separate program requires. Transportation costs can be kept quite low if one hires part-time physicians who live near the clinics and if one encourages use of public transportation. The intra-uterine device program requires very simple facilities. Equipment costs are minimal since expensive equipment or imported equipment can be carried in a bag. If large numbers of women are being served a modest service charge contributes substantially towards the expenses of the program. These are important considerations when economy is essential to meet the demand for population control as well as death control.

This discussion of mobile teams by no means excludes the necessity for a variety of service programs and means of contraception. For example, the hospital intra-uterine clinics at Yonsei, Seoul National, and Soo Do Universities in Seoul are well attended. There are many women in a city of three million who prefer the services offered by a large, reputable hospital. Other more wealthy women go to the many private clinics that offer the intra-uterine method. Then others attend government clinics in health centers and hospitals. It is also fortunate that the first condom factory began operation this year, and as condoms become widely available through the ubiquitous drugstores at a reasonable price, their easy availability will greatly benefit the many younger couples who are not coming for the intra-uterine method.

As mentioned before, one of the problems in the Korean program was to find a cold-sterilizing chemical for the plastic devices and inserters that is especially rapid, absolutely safe, and readily available. Benzalkonium chloride (*Zephiran*) is most often recommended by those who have written instructions for inserting intra-uterine devices. But *Zephiran* has some weaknesses besides the fact that it must be imported into Korea. It has a slow and incomplete bactericidal effect. It is not virucidal and soap neutralizes its action.[6,11]

There is much evidence that aqueous iodine solution provides more rapid and complete disinfection than other antiseptics available at the present time. In 1962 the National Medical Center's laboratories in Seoul tested loops and inserters that were contaminated with gram-negative and gram-positive bacteria and treated with aqueous iodine or *Zephiran*. The aqueous iodine was consistently more effective. These tests were repeated at the University of Michigan School of Public Health in September, 1964. Sections of intra-uterine devices and inserters were contaminated separately with fresh cultures of *S. aureus*, *P. aeruginosa*, and monkey feces. Separate sections were exposed to *Betadine*, aqueous iodine solution, and *Zephiran* at pH 4, 7, and 10 for varying lengths of time and various concentrations. (See table). Each entry in the table represents three tests at different pH (adjusted in tap water with NaOH or HCl). The broth was incubated for 24 hours at 37°C with *Tween 80* added. Growth of bacteria is indicated in the table if any one of the cultures was positive.

Aqueous iodine solutions have a yellow color, which is a practical advantage since the intensity of the color indicates the amount of active iodine present. The test solutions were made from U.S.P tincture, which has 2 percent iodine, 2.4 percent sodium iodide, in 47 percent alcohol. The "yellow" iodine was made by adding 0.5 cc of 2 percent iodine to 100 cc of water. The "orange" was made by adding 1 cc. (Strong tincture of iodine contains 7 percent iodine and would take about one third less to make the same solutions.) *Betadine* contains 0.5 percent iodine; the "yellow" was made by adding 1 cc and the "orange" by adding 1.5 cc to 100 cc of water. Water at pH 10 required at least 0.5 cc more tincture of iodine or *Betadine* to make the same color as the lower pH values. Thus the color indicator inherent in iodine conveniently helps one make the proper concentrations for any kind of water.

TABLE

Aqueous iodine and Zephiran disinfection of intra-uterine devices and inserters

Disinfectant: Time Minutes	*Betadine* Aq. Iodine 1: 20,000 Yellow	*Betadine* Aq. Iodine 1: 15,000 Orange	Tinct. Iodine Aq. Iodine 1: 10,000 Yellow	Tinct. Iodine Aq. Iodine 1: 5,000 Orange	*Zephiran* 1: 500 No color	*Zephiran* 1: 1000 No color
0 (control)	×	×	×	×	×	×
0.5	×	×	×	×	×	×
1	×	×	×	—	×	×
5	×	×	×	—	×	×
10	—	—	—	—	×	×
20	×	—	—	—	—	×
30	×	—	—	—	—	—
60	×	—	—	—	—	—

× indicates growth of bacteria.

The positive cultures in the *Betadine* "yellow" column are due to the fact that all the solutions were two to three hours old at this point in the experiment. The *Betadine* loses its disinfectant action quite rapidly, which is indicated by a fading of the yellow color. A fresh *Betadine* solution of proper concentration would disinfect within 10 minutes as indicated on the chart. For some reason a 1: 20,000 solution of iodine made from *Betadine* had the same color as a 1: 10,000 solution made from tincture of iodine. Thus, a fainter yellow color from tincture of iodine has greater disinfectant action and does not lose this action as rapidly as *Betadine*.

The chart indicates that a 1: 5000 solution of iodine disinfects within one minute. In actual practice a safety factor of at least 100 percent is obtained through the use of 1: 500 to 1: 2,500 solutions of iodine. Iodine contact time with scrubbed hands or clean instruments is 2 minutes or more.

The technique of disinfection used in the clinic is as follows. The intra-uterine devices, inserters, and clean gynecologic equipment are immersed for ten minutes before use. The physician does a pelvic examination with clean disinfected gloves or disposable gloves. After handscrub with soap and contact with aqueous iodine solution for two minutes, the physician places the device in the inserter and immediately inserts the device with the hands still wet from the aqueous iodine. The physician washes her hands in the aqueous iodine between cases. The nurse washes all dirty instruments in aqueous iodine to remove organic material. Then she places the instruments in the final iodine solution. Three sets of all instruments including inserters is sufficient for one physician in a busy clinic.

Aqueous iodine in the concentrations used does not stain the hands. Since iodine makes starch blue it is better to launder white coats without starch. There were no cases of iodine sensitization since iodine hypersensitivity is rare. There were no cases of irritation since simple iodine salts are noncorrosive and relatively benign in aqueous solution. There was no iodism. Iodism is a mild toxic syndrome which occurs usually after chronic ingestion of iodides. If iodism should occur among staff no treatment is required except to discontinue exposure.[7] Iodine displays a very low toxicity as compared with the high toxicity indices for *Zephiran*, mercuric chloride, and phenol.[11]

Since July, 1963, the University of Michigan School of Public Health has conducted a study using an itinerant physician to introduce an intra-uterine program in Detroit, Michigan. Detroit and suburbs has a population of approximately 2.5 million, and the city itself has 1.7 million. The city has had a 10 percent decrease in total population in the past decade, while the non-white percentage (30) has doubled. Eight percent of the total births are illegitimate. The city's population is 65 percent Catholic. The health department, due to lack of budget, gives less service to indigent mothers than it has in the past and offers no birth control services. The Planned Parenthood League tends to concentrate its activities in a single clinic downtown, with the exception of weekly clinics in three hospitals also in the downtown area and two in suburban areas. They are also sponsoring one of the clinics in this study.

Dr. Johan Eliot, Assistant Professor in the Maternal and Child Health Unit, directs this study, which aims to find out whether this type of birth control program might be effective in lower-income neighborhoods in Detroit. The clinics are conducted in specially equipped rooms in two Negro churches. The clinic offers various contraceptives (the oral, vaginal, and intra-uterine), and all new patients have a Pap smear. A physician visits each clinic once a week. Aqueous iodine solutions are used for disinfection just as in Korea. A Negro nurse and clerk who live near one of the churches conduct the educational program, schedule the women, work in the clinics and take care of most of the initial complaints of women following insertion. Wayne County General Hospital's obstetric department cooperates with the clinic by taking care of complications, such as two women who had persistent bleeding after removal and one who developed pelvic inflammatory disease. They also refer many women through systematic interviews of all women after delivery. In the last six months, one-third of the new patients at the nearest clinic were referred from this hospital. The clinic physician, except for the first few months when the nurse was being trained, receives no calls from patients and only a few each month from the nurse. The women are encouraged to call the nurse if they have any questions or problems. If any problem seems serious she can either call the clinic physician or send the woman to Wayne County General Hospital, but most problems can wait for the weekly clinic session.

There were 850 women who were given contraceptive service during the first 13 months of the program. Fifty percent received the intra-uterine device; these women had an average age of 27, with three children in eight years of marriage; 17 percent had at least one miscarriage; 15 percent were either single or separated. Thirty-five percent received the oral contraceptive and 15 percent vaginal methods; these women had an average age of 25 with two children in six years of marriage; 13 percent had at least one miscarriage and 20 percent were single or separated.

It is evident that the neighborhood clinics can reach women who need birth control services. Ninety percent of these women reported that their last pregnancy was accidental. Half of the women had never heard of the Detroit Planned Parenthood League and half gave closeness to the clinic as the most important reason they had come to this particular clinic. One of the church clinics had equal numbers of Caucasian and Negro women attending during the past seven months, while the other remained 70 percent Negro.

Loop B and loop D accounted for most insertions, with some bows and spirals also inserted. There were eight pregnancies, one with a loop D who aborted spontaneously at two months. The other pregnancies followed unnoticed expulsions. The over-all pregnancy rate was 4 per 100 woman-years. There were eight infections, all linked either to previous pelvic inflammatory disease or to contact with gonorrhea. Seven were successfully treated in the clinic with oral antibiotics after removal of the device. One patient was successfully treated at the hospital as mentioned before. Half of the women requested reinsertion after the infection cleared; however, only one has been reinserted.

The above reports indicate that an itinerant physician can introduce fairly successful intrauterine programs in medically disadvantaged areas of cities in a variety of countries. However, progress is slow in the rural areas where population is less dense, travel is tedious, and physicians are all too few. The economic situation in most underdeveloped countries is worse in the rural areas than in the cities, and this aggravates the situation. It is possible and likely that it will be necessary to modify the itinerant physician program to make even more efficient use of the physician's time. This will involve placing more responsibility on auxiliary medical personnel in the rural areas. If a well-trained nurse-midwife lived and worked in such an area, a consultant physician could visit her clinic and do the diagnostic pelvic examinations. The nurse-midwife then could do the insertions, first under the physician's supervision and later on her own, after she is well trained. She then would have to take responsibility for follow-up of the routine cases and see that those occasional women with persistent bleeding or infection are properly treated at the nearest clinic or hospital. In Pakistan, two nurse-midwives already are doing insertions under the supervision of a physician[4]. It seems likely that this is occurring elsewhere, and it will be interesting to watch these programs develop in the future.

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THE USE OF MOBILE CLINICS FOR THE INTRODUCTION OF INTRA-UTERINE CONTRACEPTIVE DEVICES

by

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The object of this study can be stated simply by quoting Dr. Guttmacher's introductory speech as chairman for the first conference on intra-uterine contraception. He said, "I was able at first hand to see the population problem and what is being done about it in India and in much of Southeast Asia. I came back with the firm conviction that the reason the restraint of population growth in these areas is moving so slowly is the fact that the methods which we offer are Western methods, methods poorly suited to their culture and to the control of mass-population growth. Our methods are largely birth control for the individual, not birth control for a nation." My own experience in rural areas confirms what Dr. Guttmacher said. Being somewhat disappointed in persuading our own masses to accept the other available methods of birth control, we undertook this trial with intra-uterine contraceptives in the hope that perhaps this may be the answer to their requirements.

It would not be out of place here to give you a picture of the countryside where this trial has been undertaken. Kaira District is situated in the western part of India in Gujarat State, which has an area of 2,670 square miles and a population of over two million. It is one of the most thickly populated areas in the country. Most of the population lives in the villages, Nadiad being the only town with a population of over 50,000. The whole district has only four qualified gynecologists and eight surgeons, who are attached to the hospitals in the small towns. The medical needs of the population are served mainly by 13 primary health centers and about 100 village dispensaries. The family planning program is being conducted by about 60 social workers attached to these dispensaries and hospitals.

There is a primary health center for a population of 80,000, with a doctor, nurse, public health nurse, and two family planning field workers. The primary health center has three subcenters, each with a midwife and family planning field worker. Before organizing a camp the medical and paramedical staff and the local doctors are given a demonstration of the device and are then requested to motivate women for insertion of intra-uterine contraceptive devices. The organization of an IUCD camp in a rural area may be represented schematically as shown on p. 61.

The technique for insertion did not differ from the one recommended by Dr. Lippes except that malignancy and pregnancy were considered as the only contraindications. Most of the insertions in this series were done by my assistants under supervision, and they could not be expected to be aware of all the diseases and have clinical experience for their diagnosis. No particular period of the menstrual cycle was preferred and the device was introduced on any day of the cycle. This practice may be objected to by others since it increases the possibility of introducing the device into a pregnant uterus, but we were forced to take this course as it was neither possible to collect the desired number of women in a village on a

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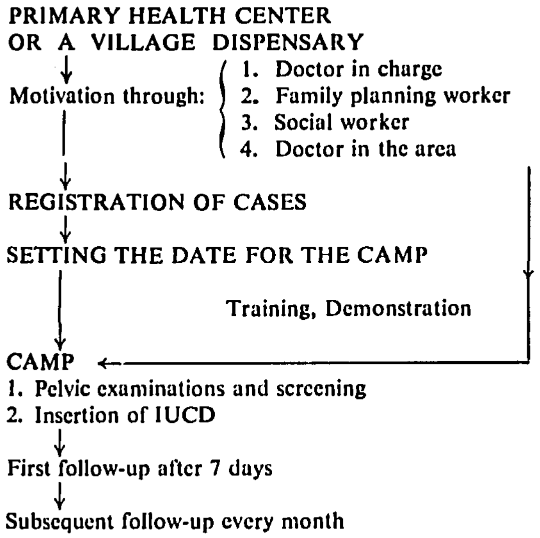

particular day of their cycle, nor feasible for us to time our visit to any particular area according to the menstrual cycle of the women there. Insertions in cases of lactation amenorrhea and abortion were done any time after 30 days.

In all cases Lippes loop size 1 was used. Though Dr. Lippes himself has advocated these small loops only for nulliparous women, we continued the trial with them under the advice and encouragement of Dr. A. Southam and Dr. S. Segal. However, in all cases of expulsion, size 1 was replaced by either size 2 or size 3. It was suggested to us by Dr. Lippes that Indian women might have comparatively small uteri. The sounding depth of uterus in 120 multiparous cases was taken, and it was found that the minimum length was 5 cm. and maximum 7.3 cm., with an average of 6.2 cm.

The clinical trial was started in February 1963, and 262 cases were given devices. Of the total number of 262 cases, 203 are active cases (i.e. women presumed to be wearing the IUCD and under observation). Fifty-nine women discontinued the method, or have been lost to follow-up, and their cases have been closed. The aggregate period of use for all cases, active and closed, is 2,480 woman-months. There has been no pregnancy with the device *in situ* in any of the cases reported here.

Table I gives the details of the 262 insertions as active and closed cases.

TABLE I

Fate of initial insertions of Lippes Loop I

Total insertions		262
Closed cases		59
Expulsions, not reinserted	7	
Removals		
Relevant	19	
Non-relevant	15	
Pregnancies	0	
Lost to follow-up	18	
Active cases		203
Aggregate woman-months of use, all cases		2,480

The majority of the cases are below the age of 30 years, with the largest group in the age range of 25-30 years. It has been our practice to advise tubectomy to all women over age 30 with more than three children and to give loops for spacing only. However, our cases include some who refused to undergo sterilization due to fear, and would be expected to use devices for a very long time. Table II gives the age groups of all cases.

TABLE II

Distribution of cases according to age

Age group	No. of cases	Percent
Below 20	3	1.1
20–25	62	23.7
25–30	89	34.0
30–35	59	22.5
Over 35	49	18.7
Total	262	100

Table III gives the distribution of these cases according to parity. It is very unusual, except in the highly educated classes, for nulliparous women to use any method of birth control. The three nulliparas in this series are recently married working women who wish to avoid conception. This table includes a number of women who have 3 or 4 children, but do not want to undergo sterilization, and wish to avoid pregnancy by using the IUCD. Although women of parity of 6 and over 6 are using the device, it must be remembered that infant mortality has been very high; very few of these women have the desired number of children, or what is more important, the desired number of sons. In India very few women would like to have fewer than two sons, no matter how many daughters they have.

TABLE III

Distribution of cases according to parity

Parity	No. of cases	Percent
0	3	1.1
1	16	6.1
2	46	17.5
3	38	14.5
4	52	19.9
5	39	14.9
6	28	10.7
Over 6	40	15.2
Total	262	100

In these 262 insertions there have been 16 expulsions in 14 cases, two expelling the device twice. The device was reinserted in 7 cases, while 7 cases refused reinsertion on the grounds that it might be expelled again. Besides, it is not always possible for Indian village women to visit hospitals or dispensaries without the knowledge of elders in the family who might oppose the use of the devices. Five of the 16 expulsions were unnoticed and two were followed by unintended pregnancy, one after 4 months and another after 11 months of use. Table IV shows the duration of use before expulsions occurred.

TABLE IV

Incidence of expulsion

Months since insertion	No. of expulsions		
	Noticed	Not noticed	Total
0–1	2	3	5
1–2	2	–	2
2–3	1	–	1
3–4	–	–	–
4–6	2	1*	3
6–9	3	–	3
9–12	–	1*	1
Over 12	1	–	1
Total	11	5	16 (6.1%)

* Expulsion followed by unintended pregnancy

Indian women are, on the whole, accustomed to and tolerant of certain complaints during menstrual periods. However, in certain cases after insertion of devices, the complaints of heavy bleeding during menstruation, backache, and abdominal pain became very severe, requiring removal in 19 cases (7.3%). The maximum incidence of such complaints has been either in the first two months after insertion or after one year. In the 8 cases where the device was removed between 3 and 6 months after insertion, side effects occurred earlier, but the device was not removed immediately in the hope that after a few periods bleeding would return to normal. Table V gives the details of cases where the device had to be removed due to severe side effects.

Besides severe side effects which required removal of the device in 19 cases, many patients complained of minor side effects. Many of these complaints have been subjective, since women

TABLE V

Removals for relevant reasons, by duration in situ

Reason for removal	Months since insertion								
	0–1	1–2	2–3	3–6	6–9	9–12	Over 12	Total	Percent
Bleeding	3	2	–	9	–	–	3	16	6.1
Backache	1	–	–	–	–	–	–	2	0.8
Abdominal pain	–	1	–	–	–	–	–	1	0.4
Total	4	3	–	9	–	–	3	19	7.3

in the interior areas are prone to blame the device for any ailment they may develop. The most common complaint has been excessive vaginal discharge, which did not require removal of the device.

Such minor side effects have been classed either as post-insertion (i.e. occurring up to the onset of the first period after insertion, or up to one month in cases of lactation amenorrhea) or later (i.e. after the first menstrual period or one month, as the case may be). None of these cases required any specific treatment. Table VI gives the details of such minor side effects. Some cases reported both post-insertion and late side effects, and these cases are included in both groups.

TABLE VI

Minor side effects not requiring removal

Complaint	Time complaint occurred		
	Post-insertion	Later	Total
Bleeding	12	16	28
Spotting	5	–	5
Backache	6	8	14
Cramps	1	–	1
Vaginal discharge	15	22	37
Total	39	46	85

From Table VI it will be seen that the main side effect has been excessive vaginal discharge, which we attribute to poor hygiene. The sanitary environment in this group is very poor and a sense of personal hygiene practically negligible. In order to evaluate this complaint the vaginal smears of 34 cases were examined; smears had also been taken before insertion of the device, and we hope to evaluate this side effect in further detail.

TABLE VII

IUCD insertions, by duration and aggregate woman-months of use

Months since first insertion	Total cases	Active cases	Closed cases	Woman-months of use
0–1	5	5	0	3
1–2	13	12	1	18
2–3	13	11	2	31
3–6	38	29	9	121
6–9	35	25	10	230
9–12	33	23	10	273
12–15	55	47	8	664
15–18	33	23	10	558
Over 18	37	28	9	582
Total	262	203	59	2,480

Table VII gives total cases, active cases, and closed cases, by duration and aggregate woman-months of use since first insertion.

It has been already mentioned that, contrary to the recommendations of various workers, we have not considered any one period of the menstrual cycle as the most suitable period for the insertion of the device. Though this was done for our own convenience, the comparative results of insertion in different phases of the menstrual cycle have been quite revealing. The incidence of removal due to side effects has been highest in cases where the device was inserted during the first 14 days of the cycle, and lowest in cases of lactation amenorrhea. Expulsion rates do not show much variation but have also been highest in cases where the device was inserted during the first 14 days of the menstrual cycle. Other side effects have been few (only in 7 percent of the cases) where the device was inserted after the first 14 days of the menstrual cycle, while insertion during the first 14 days increased the incidence of side effects to 28 percent. Comparative data for three phases are given in Table VIII.

TABLE VIII

Side effects in relation to time of insertion

Time of insertion	No. of cases	Removal due to side effects	Expulsion	Other side effects
Lactation amenorrhea	102	4 (3.9%)	6 (5.9%)	19 (18.5%)
Within 14 days after menses	102	10 (9.8%)	7 (6.8%)	29 (28.5%)
Later than 14 days after menses	58	5 (8.6%)	3 (5.0%)	4 (7.0%)

Conclusions

This trial was undertaken to assess the possibility of mass use of intra-uterine contraception by village women through medical and para-medical personnel. Limiting its use to specialists would make it a birth control method for individuals and not for a nation as is desired. In India specialists cannot be found to do this job. Although our experience with a small number of cases is not conclusive, we consider that the use of the Lippes loop may be an answer to the requirements of countries like India.

COMPARATIVE MERITS OF THE SPIRAL, LOOP, AND BOW: A SURVEY OF 11,833 WOMAN-MONTHS OF EXPERIENCE AT SLOANE HOSPITAL

by

ROBERT E. HALL, M.D.*

The purpose of this paper is to present data obtained in an evaluation of intra-uterine contraceptive devices at the Sloane Hospital for Women, in New York City.

Case material

Figure 1 illustrates the types of the devices used, and the number of insertions is presented in Table I. One hundred and one of the total insertions were performed on private patients, 1,807 on clinic patients. All but four of the patients had experienced at least one pregnancy.

The duration of time from each insertion or reinsertion up to September 1, 1964, or until pregnancy, removal, or expulsion occurred, is represented by Figure 2. The aggregate experience with spiral 5 is 3,587 woman-months; with loop 1, 570 woman-months; with loop 2, 3,802 woman-months; with bow 3, 3,503 woman-months; with bow 5, 371 woman-months; and with all of the devices, 11,833 woman-months. As indicated by Figure 2, the spiral and loops 1 and 2 have been used with varying frequency for 17 months, whereas bow 3 has been used for only twelve months and bow 5 for three months. Since loop 1 has been found to be too small for the parous uterus, this device has been electively removed whenever possible.

Of the 1,771 patients who applied for intra-uterine contraception, 57 were refused for the following reasons: recent pelvic infection (18), suspected pregnancy (12), fibromyomata uteri (6), cervical stenosis (4), and other reasons (17). Subsequent insertions were made in 19 of these cases.

TABLE I

Insertions, April 1963 through August 1964

	Spiral 5	Loop 1	Loop 2	Bow 3	Bow 5	Total
New insertions	346	51	592	555	189	1733
Reinsertions	16	9	54	73	23	175
Total insertions	362	60	646	628	212	1908

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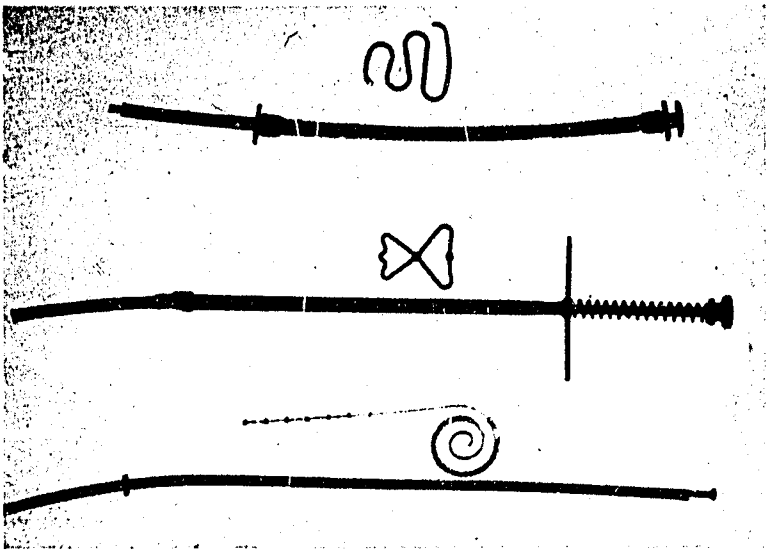

Fig. 1. Top: Lippes loop and inserter. Center: Birnberg bow and inserter. Bottom: Margulies spiral and inserter. Numerical designations in text refer to sizes : loop 1 — 25 mm; loop 2 — 31 mm; bow 3 — small ; bow 5 — regular ; spiral 5 — regular.

Insertion of the device was performed in the vast majority of cases six weeks after delivery or abortion. The insertions were made without regard to the phase of the patients' menstrual cycles.

Aside from soaking the devices and their inserters in 1:1000 solution of benzalkonium chloride for at least 20 minutes, sterile precautions were not observed. The devices were loaded into their inserters with clean bare hands. Pelvic examination was performed, the inserter introduced into the cervical canal, and the device extruded into the uterine cavity. The stem of the spiral was cut squarely against one of its beads, leaving only one or two beads protruding into the vagina; the threads of the loop were shortened so that only about one inch protruded. In about 20 percent of the cases it was necessary to grasp the cervix with a tenaculum and to dilate the canal with a No. 13 Hanks dilator. Pain was rarely experienced by the patients.

Each patient was given a list of written instructions describing the possible side effects and the home remedies that might alleviate them. With severe symptoms the patients were asked to return to the clinic immediately; otherwise they were scheduled for a follow-up visit in one year.

Incidence of complaints

Each complaint by a patient was recorded for statistical analysis by Dr. Tietze of the National Committee on Maternal Health. The incidence of these complaints is presented in Figure 3 in relation to the time interval between insertion of the device and registration of the complaint. The incidence of specific complaints, calculated as a cumulative rate per 100 patients during the first twelve months after insertion, is presented in Table II.

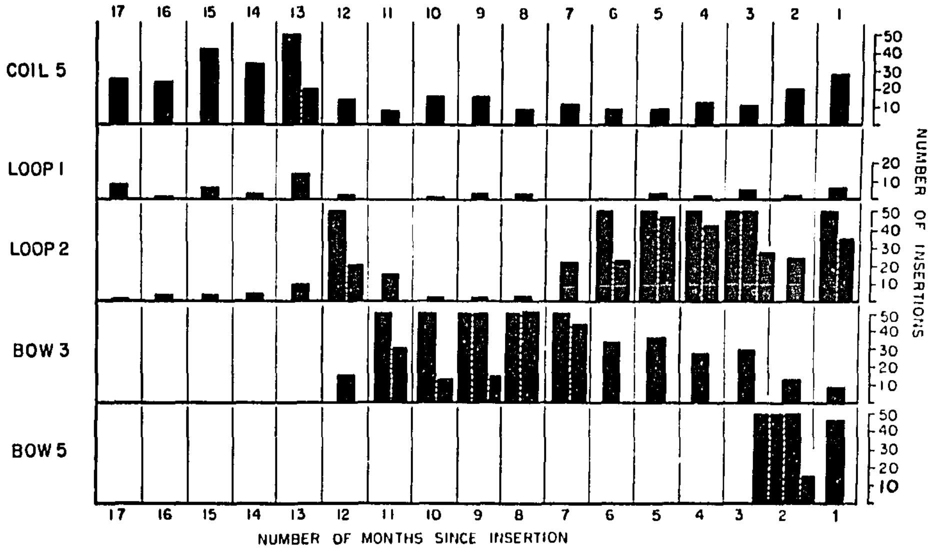

Fig. 2. Duration of experience with intra-uterine contraceptive devices, to September 1, 1964

TABLE II

*Cumulative incidence of specific complaints**

	Spiral 5	Loop 1	Loop 2	Bow 3
Bleeding	47.9	29.8	20.8	16.1
Pain	22.1	11.9	9.7	4.5
Excess beads protruding	13.1	—	—	—
Inability to feel though palpable	4.0	4.1	8.6	—
Inability to feel, IUCD *in utero*	1.7	6.1	0.7	—
Husband's complaints	5.2	—	0.2	—
Miscellaneous	10.3	4.1	8.2	6.2
Infection	4.0	4.0	1.0	1.0
Complete expulsion	12.4	14.2	8.7	4.1
Partial expulsion	3.7	7.7	0.9	0.4
Pregnancy after insertion	2.1	9.9	1.2	4.2
Pregnancy before insertion	0.3	—	—	0.4
Suspected pregnancy	0.7	—	0.7	0.6
Any complaint	63.1	54.6	36.9	24.9

* Cumulative rates per 100 patients during first 12 months after insertion, computed by Modified Life Table Procedure.

Complications

The fates of first insertions and all insertions are indicated in Table III.

The incidence of expulsions following first and second insertions of the devices is shown in Table IV. The type of device reinserted after an initial expulsion was usually different from that originally inserted.

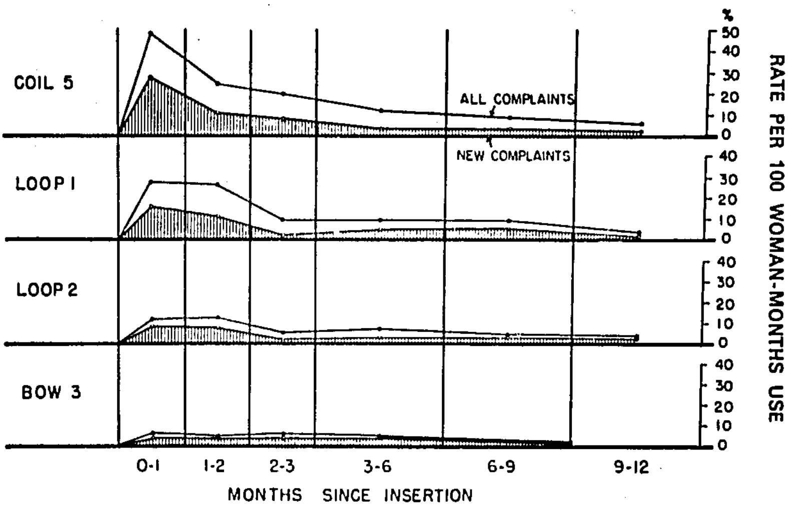

Fig. 3. Incidence of complaints related to time interval after insertion.

TABLE III

Fate of first insertions and all insertions

	Spiral 5 No. (%)	Loop 1 No. (%)	Loop 2 No. (%)	Bow 3 No. (%)
First insertions	346	51	592	555
Expulsions	58 (17)	12 (30)	35 (6)	11 (2)
Removals	90 (26)	21 (41)	28 (5)	35 (6)
Pregnancies	7 (2)	4 (8)	7 (1)	29 (5)
Devices *in situ* without pregnancy	191 (55)	14 (27)	522 (88)	480 (86)
Total insertions	362	60	646	628
Expulsions	64 (18)	18 (30)	41 (6)	15 (2)
Removals	92 (25)	22 (37)	30 (5)	43 (7)
Pregnancies	9 (2)	4 (7)	7 (1)	34 (5)
Devices *in situ* without pregnancy	197 (54)	16 (27)	568 (88)	536 (85)

TABLE IV

Expulsions after first and second insertions

	Spiral 5	Loop 1	Loop 2	Bow 3	Total insertions	Total expulsions
First insertions	346	51	592	555	1544	
Expulsions	58 (17%)	12 (24%)	35 (6%)	11 (2%)		116 (7%)
Second insertions	11	9	21	38	79	
Expulsions	5 (45%)	7 (78%)	4 (19%)	2 (5%)		18 (23%)

The over-all incidence of removals is cited in Table III. The reasons for these removals are given in Table V. One hundred of the 174 initial removals (58%) were necessitated by bleeding and/or pain; 25 were not medically indicated; 13 were elective. In most of the 72 cases where a device was reinserted after removal, a different device was used for reinsertion, as shown in Table VI.

TABLE V

Reasons for removals

	Spiral 5	Loop 1	Loop 2	Bow 3	Total
Bleeding	41 (43)[*]	1	5	7	54 (56)
Bleeding and pain	17	1	8 (9)	6 (7)	32 (34)
Pain	5	0	4 (5)	5 (10)	14 (20)
Infection	6	1	2	2	11
Psychological	9	0	4	7	20
Surgery	1	3	1	0	5
Moving away	3	0	0	2 (4)	5 (7)
Accidental	1	0	1	0	2
Suspected pregnancy	1	1	0	0	2
Desire to conceive	4	1	3	6	14
Husband's insistence	1	0	0	0	1
Elective	0	13 (14)	0	0	13 (14)
Tail embedded	1	0	0	0	1
Total	90 (92)	21 (22)	28 (30)	35 (43)	174 (187)

[*] Unbracketed numbers represent first removals, bracketed numbers represent total removals.

TABLE VI

Reinsertions following removals, by type of device

Device removed				
Spiral 5	Loop 1	Loop 2	Bow 3	Device reinserted
2	0	0	0	Spiral 5
0	0	0	0	Loop 1
13	12	2	1	Loop 2
24	2	4	0	Bow 3
5	2	3	2	Bow 5

The pelvic infections encountered in these cases are described in Table VII. Nineteen of the 30 infections were either questionable or mild. The fever exceeded 102.8°F in only two; the temperature returned to normal within 48 hours in every case but one. Nine of the infections occurred less than nine weeks after insertion, eight between nine and twenty weeks, and thirteen more than twenty weeks after insertion.

TABLE VII

Infections

	Spiral 5	Loop 1	Loop 2	Bow 3	Total
Number of infections	14	3	5	8	30
Patient hospitalized	2	1	3	1	7
Antibiotic therapy	9	3	3	4	19
Device removed	8	1	2	4	15
Previous pelvic infection	2	1	1	1	5
Severity of infection					
Questionable			1	1	8
Mild			2	5	11
Moderate	4	1	2	2	9
Severe	2	0	0	0	2

Dr. Tietze's calculations from the Sloane Hospital data through June 30, 1964, show cumulative unintended pregnancy rates, with the device *in situ* or with the site of the device undetermined, of 2.1, 1.2, and 4.2 per 100 cases during the first twelve months after insertion of the spiral, loop 2, and bow (see Figure 4) respectively. The number of unintended pregnancies seen through August 31, 1964, are shown in Table VIII, the outcome of these pregnancies in Table IX, and the fate of the devices following conception in Table X.

TABLE VIII

Unintended pregnancies, through August 31, 1964

	Spiral 5	Loop 1	Loop 2	Bow 3
Device *in situ*	7	4	6	11
Device undetermined	0	0	1	22
Unnoticed expulsion	2	0	0	1
Pregnant before insertion	1	0	0	4
Pregnancy suspected, not proven	0	0	1	2
Total pregnancies	10	4	8	40

TABLE IX

Outcome of pregnancies with device in situ *or undetermined*

Term births, living children	6
Premature birth, neonatal death	1
Spontaneous early abortions	9
Therapeutic abortions	3
Criminal abortion	1
Ectopic pregnancies	2
Known current pregnancies	17
Presumptive current pregnancies	12

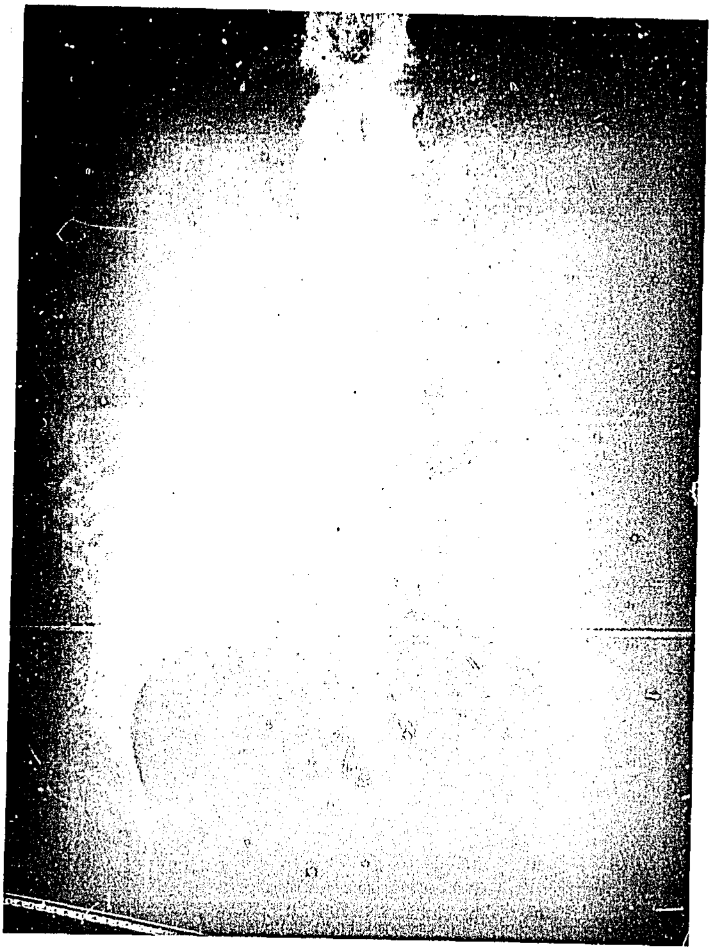

Fig. 4. Birnberg bow *in situ* in pregnant uterus, in contact with fetal cranium.

TABLE X

Fate of devices in unintended pregnancies

	Spiral 5	Loop 1	Loop 2	Bow 3	Total
Presumably *in utero*	0	0	0	25	25
In utero	0	0	2	1	3
Expelled during pregnancy	0	2	2	2	6
Removed during pregnancy	7	1	1	0	9
Expelled or removed at abortion or delivery	1	1	2	9	13

Other complications occurred. In one case a loop 2 was displaced within the peritoneal cavity (see Figure 5). It is not known whether this displacement occurred at the time of insertion or during attempts to remove the device. Although the loop lay in the cul-de-sac

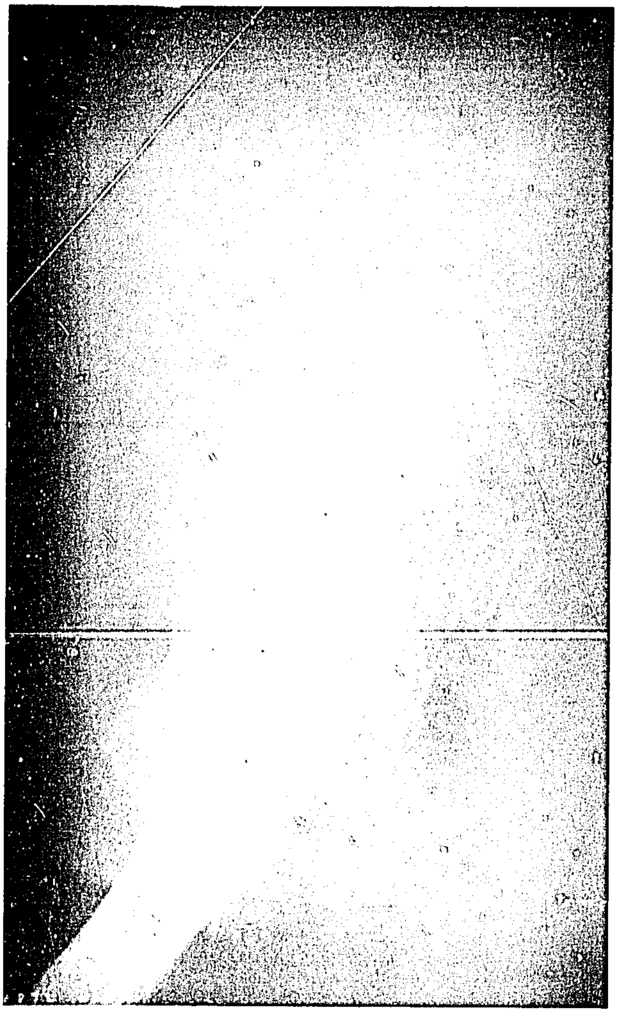

Fig. 5. Displacement of Lippes loop within the peritoneal cavity.

and could probably have been removed through a posterior colpotomy incision, surgical interference was refused by the patient.

At the time of annual checkup, the terminal bead of the coil was found to be embedded beneath the vaginal mucosa of one patient (see Figure 6) and beneath the cervical mucosa of another. Attempts to remove these beads by traction on the device resulted in avulsion in both instances, necessitating their excision under local anesthesia.

Cost

At present the manufacturer's list price for 20 intra-uterine contraceptive devices, one inserter, and whatever other equipment is necessary for insertion and removal, is $50.40 for the spiral, $58.60 for the loop, and $55.00 for the bow. The cost of additional devices is $1.20 per spiral, $2.50 per loop, and $1.95 per bow. It is said that physicians charge as much as

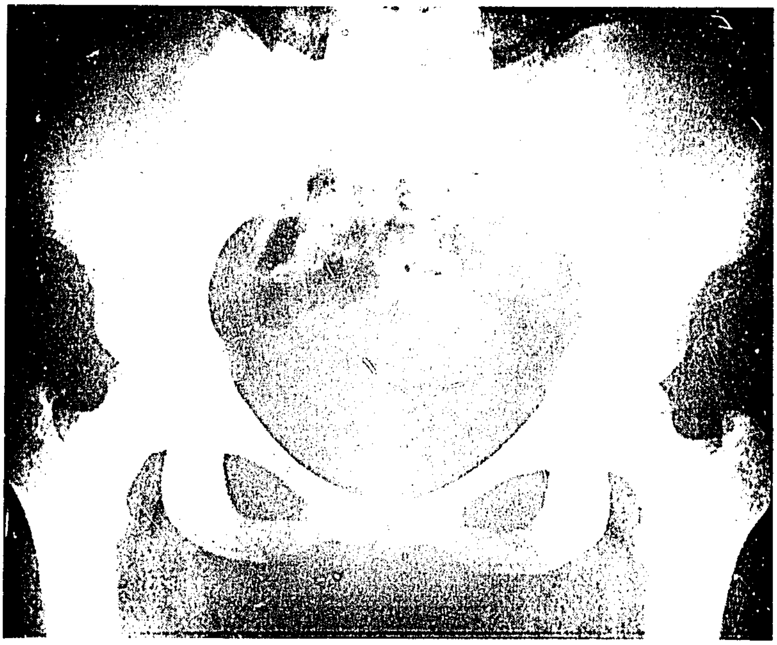

Fig. 6. Terminal bead of coil embedded beneath the vaginal mucosa.

$100.00 for the insertion of these devices. Needless to say, the future of intra-uterine contraception will be imperilled by equipment costs and professional fees of this magnitude.

Conclusions

Table XI gives the cumulative rates of complications, side effects, expulsions, and pregnancies. From this table and the foregoing information, the following conclusions seem warranted with regard to the comparative merits of the various plastic devices used in this study:

1. Although the pregnancy rate with the spiral is low (2.1%), the rates of total side effects (63.1%), major side effects (25.4%, or 56.6% of the total), and first expulsions (16.1%) are so high that further use of the spiral should probably be abandoned.

TABLE XI

Cumulative rates of complications*

	Spiral 5	Loop 2	Bow 3
Total side effects	63.1	36.9	24.9
Major side effects**	25.4 (56.6)***	8.3 (31.8)***	5.8 (35.8)***
First expulsions	16.1	9.3	4.5
Unintended pregnancies	2.1	1.2	4.2

* Cumulative rates per 100 patients during first 12 months after insertion, computed by Modified Life Table Procedure.

** Side effects sufficiently severe to warrant removal of the device.

*** Ratio of major to total side effects.

2. It is already known that loop 1 is unsuitable for the parous woman. The comparatively low rates of pregnancy (1.2%), total side effects (36.9%), major side effects (8.3%, or 31.8% of the total), and first expulsions (9.3%) suggest that loop 2 is the most acceptable plastic device now available.

3. With bow 3 the rates of total side effects (24.9%), major side effects (5.8%, or 35.8% of the total), and first expulsions (4.5%), are eminently satisfactory, but the pregnancy rate (which is actually higher than the 4.2% indicated, because 13 additional pregnancies have been discovered in the two months since Dr. Tietze's analysis) is so high that the use of bow 3 in parous women should be discontinued. Further study is needed in order to determine whether the pregnancy rate will be lower with bow 5.

EXPERIENCE WITH INTRA-UTERINE DEVICES IN PUERTO RICO

by

ADALINE P. SATTERTHWAITE, M.D., EDUARDO ARANDES, M.D.
and MARIA E. NEGRON, M.D.*

New inert polyethylene plastics, antibiotics, and the pressure of population in economically underdeveloped areas of the world, have all combined to stimulate interest in intra-uterine contraception. After four years of experience with oral progestagens[8] in rural Puerto Rico, in November 1961 we began testing the Margulies spirals[6] and Lippes loops.[5] We have participated in the cooperative statistical study conducted by the National Committee on Maternal Health as reported at this conference by Dr. Tietze.

As of September 1, 1964 we had accumulated 15,419 woman-months of experience with 1,531 primary insertions. Two-thirds of the women are from rural or semi-rural areas; two-thirds are between the ages of 20 and 29; one-half of them have two to four children and one-quarter have six or more children.

Table I shows the number of first insertions, total insertions, active cases, and aggregate woman-months of use as of June 30, 1964, for the clinics based at Humacao.

TABLE I

First insertions, total insertions, active cases, and aggregate woman-months of use, by type of device

Type of device	First insertions	Total insertions	Active cases	Woman-months of use
Large spiral	299	345	170	3,216
Small spiral	200	235	97	2,429
Large loop	357	456	334	3,384
Small loop	227	255	62	3,024
Other devices	77	105	57	917
Total	1,160	1,396	720	12,970

It will be noted that the large spiral and the large loop represent the largest groups of cases. In the past year we have discontinued insertions of the smaller devices for reasons which will become evident shortly. Other devices include the smaller tailless Margulies spiral, the Birnberg bow [1,3], and nylon rings. The total number of active cases, 720, represents only 62 percent of the series, but (looking at Table II) if we consider the number still active for each of the large devices compared with the number of primary insertions, we find that 83 percent are active for the large loops and only 50 percent for the large spirals.

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TABLE II

Percentage of women with primary insertions still using the same device

Type of device	Primary insertions	Active	
		No.	%
Large spiral	299	148	50
Large loop	357	296	83
Total, all devices	1,160	720	62

The better acceptance for the large loops is so apparent that it is now virtually impossible to convince the physicians working with me to use the spirals, even for the sake of the study design.

It is the accidental pregnancies, the spontaneous expulsions (especially those that are unnoticed), and the removals for medical reasons (i.e. bleeding, pain and discharge), which reduce the effectiveness of this method. Let us further examine the statistics.

In Table III we see that there were 40 unintended pregnancies in the series, 25 with the device *in situ* and 15 with the device undetermined.

TABLE III

Unintended pregnancies, with device in situ *and undetermined, by type of device: numbers and cumulative rate per 100 cases during first year after insertion*

Type of device	Number of pregnancies			Rate per 100 cases	Cooperative study Rate per 100 cases
	Total	*In situ*	Undetermined		
Large spiral	4	2	2	0.4	1.1
Small spiral	11	8	3	6.4	3.0
Large loop	6	4	2	1.5	1.3
Small loop	18	10	8	6.8	5.5
Plastic bow					5.5
Steel ring					3.6
Other devices	1	1		NC	2.3
Total	40	25	15	NC	2.6

NC = Not computed

Some of the latter undoubtedly represent pregnancies following unnoticed expulsions. It will be noted that our experience very closely parallels that of the entire series. Again it is evident that the larger devices offer better protection. We first discontinued the small loop because of the number of accidental pregnancies. However, it should be emphasized that these 18 pregnancies, with the single exception of one early abortion, were carried to term with the delivery of normal infants and the expulsion of the loop with the membranes or the placenta. There was one tubal pregnancy in a woman with a small loop in the uterus. An intra-uterine pregnancy followed this misadventure with the loop still *in utero*. After delivery the patient was sterilized.

With the small spiral, the pregnancy rate per 100 cases during the first year after insertion was 6.4 in our series: essentially the same as that for the small loop. However, our experience with the termination of the pregnancies was much different and gave cause for alarm. There were eight pregnancies with the device *in situ*. In two, the diagnosis of pregnancy was made early, before retraction of the tail; the device was removed without difficulty and the pregnancy continued uneventfully to term. In the other six cases the devices could not be removed. Three of these aborted, two in the first trimester and one at five and a half months. This patient had such severe pain and occult hemorrhage that she required hospitalization and blood transfusions before she finally aborted. The tail of the spiral was embedded in a large retroplacental clot. A fourth pregnancy carried to seven and a half months and required cesarean section for *abruptio placentae*, also with fetal loss. Only two women pregnant with the small spirals *in utero* successfully carried to term. The babies were normal.

With the large spiral *in situ*, one of the accidental pregnancies aborted at two months; in the other the device was removed successfully and the pregnancy is proceeding normally.

With the large loop *in situ* there have been four accidental pregnancies. Two have aborted in the first trimester; one woman was delivered vaginally of a living premature infant (33 weeks, weight 4 pounds), but delivery was preceded by painless third-trimester bleeding, requiring hospitalization, for a week before spontaneous onset of labor. Marginal *placenta previa* was diagnosed. The large loop was lying free on the maternal surface of the placenta. In the fourth case, the suture of the device was still visible vaginally when pregnancy was diagnosed. The device was removed without difficulty and the pregnancy continued uneventfully to term.

In the case of the spirals and the large loop it would appear that the device should be removed as soon as pregnancy is suspected, in order to favor an uneventful termination. We have five such cases where the device was removed and the pregnancy continued to term, four with the tailed spirals and one with the large loop. In no instance was an abortion provoked by removal of the device. This is another reason for favoring the tailed devices, and for leaving the vaginal appendage as long as possible. With the suture of the large loops, one to two centimeters may extend from the cervix without causing any annoyance; this is not true of the tail of the spirals.

TABLE IV

First expulsions, noticed and unnoticed, by type of device; numbers and cumulative rate per 100 cases during first year after insertion

Type of device	Number of expulsions: Total	Noticed by patient	Unnoticed by patient *	Rate per 100 cases	Entire study Rate per 100 cases
Large spiral	62	57	5	23.2	17.6
Small spiral	45	40	5	24.6	30.0
Large loop	25	17	8	8.5	9.0
Small loop	64	36	28	26.0	13.3
Plastic bow					3.8
Steel ring					8.7
Other devices	13	11	2	NC	12.8
Total	209	161	48	NC	13.8

* Excluding expulsions followed by conception.

NC = Not computed.

In Table IV we see that the expulsions, noticed and unnoticed, are significantly lower for the large loop: 8.5 per 100 cases during the first year after insertion. Some women are chronic ejectors, perhaps due to an unusually irritable uterus or to incompetence of the internal cervical os. In any event, we have found that 50 percent of the women who expel the first device will retain the second. But if the woman expels the second time the chance of retaining a third device is so small as to make it advisable to change contraceptive methods. From the entire series the plastic bows appear to have the lowest expulsion rate: 3.8. Actually we have been using the plastic bow in chronic ejectors and have had some measure of success. This practice, however, has disadvantages from a public health point of view. The bow is more difficult to insert, requiring some cervical dilation, and its follow-up depends on X-ray or repeated sounding of the uterine cavity to ascertain its continued presence. Removal is also more difficult than with devices which have a vaginal appendage.

In Table V we note that, in our series at least, the removals of large loops for medical reasons were 7.2 per 100 cases during the first year after insertion, significantly less than with the other three devices. These removals are approximately 4 percent for bleeding and 3 percent for pain, discharge, and infection.

TABLE V

Removals for medical and personal reasons, by type of device: numbers and cumulative rates per 100 cases during first year after insertion

Type of device	Medical reasons			Personal reasons		
	Number	Rate	Entire study rate	Number	Rate	Entire study rate
Large spiral	41	16.1	14.2	17	5.6	2.1
Small spiral	22	12.1	11.9	13	6.3	4.3
Large loop	18	7.2	11.8	8	3.6	2.3
Small loop	36	11.5	13.3	13	6.1	2.8
Plastic bow			8.9			1.0
Steel ring			4.7			0.8
Other devices	7	NC	10.1	3	NC	2.3
Total	124	NC	11.0	54	NC	2.1

Most women have bleeding for one to ten days after insertion, and continue spotting off and on until the next menses, which is heavier than usual. About 20 percent of women will continue spotting in the second month, and may continue to have excessive menses for several months. Actually the removals for bleeding were not because of alarming hemorrhage, but rather for persistent and annoying sero-sanguinous discharge and spotting, requiring constant vigilance on the part of the woman. These complaints are twice as frequent with the large spirals as with the large loops.

Another difficulty with the spiral is the contraction of the uterus following menses, with the protrusion of several beads of the tail. In spite of our warning the women of this eventuality, they come rushing back to clinic thinking that the device is coming out. Some physicians unfamiliar with the method, upon seeing four or more beads outside the cervix, conclude that the device is being expelled and remove the device instead of cutting off the excess tail. This is another disadvantage of the stiff tail in an unsophisticated population, especially in view of their aversion to self-examination.

The presence of a rather disagreeable discharge in the first month is not surprising when one considers the insult to the endometrium. This reaction of fibrin and mononuclear infiltration is seen in the hysterectomy specimens removed a week or two after insertion[7]. In the specimens studied after the first menses there is much less reaction noted.

We warn the women that they must expect spotting and discharge and discomfort in the first month, and provide them with 8 or 12 tablets of methergen in case of excessive bleeding; there are few complaints and very few return to clinic before the next appointment. About half the women use the methergen. In a few women, parenteral administration may be necessary to control bleeding. Again, it should be mentioned that these complaints are 50 percent less frequent with the large loop than with the large spiral.

We are now seeing the women with the large loops one month to six weeks after insertion and not again until after six months. Almost always those with the large spirals come ahead of time with a number of complaints – the commonest being spotting, pain, and discharge.

Pain is a frequent complaint with the large spiral, especially when there has been a long interval since the last pregnancy. Women postpartum have very little discomfort on insertion and those lactating have no problem with discharge and bleeding. In only two instances did we try insertion in nulliparas and found this a very painful procedure. There may be syncope associated with intra-uterine manipulation even in the absence of severe pain.

Although 1.6 percent of patients discontinued intra-uterine contraception because of "infection" diagnosed by the physician in attendance, who made the decision to remove the device, there were only three instances of acute infection associated with elevated temperature, acute tenderness, purulent discharge, and leukocytosis. The infections occurred within a week of insertion. Two were postpartum. All three were treated with removal of the device and antibiotics, and two of the three were hospitalized. After recovery all three women rapidly became pregnant and delivered normally. All three had past histories of chronic pelvic inflammatory disease and probably should have been excluded from the study, although at the time of insertion they presented no evidence of active infection. Milder exacerbation of pelvic inflammation may be treated with antibiotics without removal of the device.

A large proportion of our patients have acute or chronic cervicitis, monilial or trichomonal vaginitis. In spite of the local inflammatory lesions we do insertions and prescribe appropriate treatment. We defer cauterizations of the cervix until the second or third visit. It would be ideal to treat the local condition first and insert the device at a later time, but with our clinic population this is not practicable. We must protect while there is still time and while the motivation is high.

We have done Papanicolaou smears at insertion and repeated them at six-month intervals, or oftener in the case of anaplasia. Women with suspicious smears have been biopsied. None of our women wearing the devices have developed cancer *in situ* or invasive cancer. There was one patient who had cancer *in situ* at insertion and who was subsequently treated by total hysterectomy.

We have done endometrial biopsies on insertion in 1,002 women. We found that of the 202 postpartum insertions, 116 (57%) showed "endometritis." Of the non-postpartum insertions 42 (5.2%) showed endometritis. In 199 cases we have subsequent biopsies that were obtained upon (1) expulsion of the device and reinsertion; or (2) removal of the device for personal reasons – desire for pregnancy or separation from spouse – or to exchange for a larger more protective device; or (3) removal for bleeding, pain or discharge. These results are shown in Table VI.

We can only comment on the non-relevant removals as the group in which there were no complaints relative to the method. It will be noted that in the postpartum endometritis group at insertion, there were 10 non-relevant removals, of whom 20 percent still showed endometritis. In the non-postpartum endometritis group at insertion there were 5 non-relevant removals and 40 percent showed endometritis. In the normal group there were 80 removals and 23 percent showed endometritis. Biopsies taken at removal within 6 months following insertion showed 22 percent endometritis, while those with the device *in utero* from 18 to 24 months showed only 7 percent endometritis. It is interesting that none of these patients had symptoms, in spite of the microscopic evidence of inflammatory reaction. We must admit that our sample is too small to have much statistical significance, but our findings do suggest that postpartum endometritis is of less importance than non-postpartum endometritis. It might be worthwhile to do random follow-up biopsies on a number of women wearing devices at different times in the menstrual cycle. Most of the pre-insertion biopsies were done in the proliferative phase.

TABLE VI

Follow-up on 199 endometrial biopsies after a total of 2,750 months in utero

Initial pre-insertion biopsy	Biopsy repeated after						
	Expulsion		Relevant removal		Non-relevant removal		Total biopsies
	Endometritis		Endometritis		Endometritis		
	Positive	Negative	Positive	Negative	Positive	Negative	
Endometritis							
Postpartum	2	4	2	8	1	3	20
Not postpartum	1	3	2	3	2	4	15
No Endometritis	4	43	15	65	17	20	164

After discontinuing intra-uterine contraception, 84 women have become pregnant, the average elapsed time for those at risk between termination of contraception and conception being 6 months. Sixty have delivered normal infants at term; there was one stillborn at term, cause not known; 20 are now pregnant and 3 have aborted. Eight women have returned for reinsertion postpartum.

Compared with the protection offered to the individual well-motivated woman who uses oral contraceptives, the intra-uterine devices are less effective. However, when one considers use-effectiveness in a public health situation, the intra-uterine devices have the advantage of continuing protection after a single non-repetitive action. There is a definite psychological advantage for many women in that the protection is provided by a third party unrelated to the sexual act. In Humacao we offered a "cafeteria choice," but the two most popular methods in the past two years have been the orals and IUCD. From November 1, 1961 to November 1, 1963, 600 women chose oral progestagens and 608 chose the IUCD. As shown in Table VII, there was some difference in age and parity of the two groups; but even taking this into consideration it is obvious that intra-uterine contraception provides more continued protection.

If we had used the large loops from the beginning of our series we might have been able to have 83 percent continuing users. In view of the physicians' time involved, the small initial cost of the IUCD, and the expense of frequent follow-up visits to the women who fail to return in time for the pills, the IUCD is a much more economical measure for protection from pregnancy than the oral progestagens.

TABLE VII

Comparison of women by contraceptive method chosen

	Intra-uterine device	Oral contraceptive
Number of women	608	600
Percent over 30 years of age	24	12
Percent with 4 or more children	40	25
Percent active at end of two-year period	70	43

In another voluntary clinic opened recently in the metropolitan area, where only IUCD are being offered, we are finding that we can give protection to a large number of women at a minimum expense of time and effort. The rate of admissions to this clinic in the 6 months since its opening has increased fivefold. This has been achieved in the deliberate absence of any effort at publicity; the satisfied women have just been bringing their friends.

Conclusions

Intra-uterine contraceptive devices have been used by 1,160 Puerto Rican women, with 12,970 woman-months of observation since November 1961. The large loop has been found to be the most acceptable and effective, with minimal complaints and complications referable to the device. Accidental pregnancies have been 1.5 per 100 cases; expulsions 8.5 per 100 cases; and removals for medical reasons (mainly bleeding and pain) 7.5 per 100 cases during the first year of insertion. If accidental pregnancy with device *in utero* is diagnosed, prompt removal of the device is recommended to favor an uneventful prenatal course and normal delivery. Eighty-three percent of the women who had primary insertions with the large loop are still continuing its use. From a broad public health viewpoint, IUCD, especially the large loops, offer a promising means of population control.

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INTRA-UTERINE CONTRACEPTION IN THE POSTPARTUM PATIENTS OF A LARGE MATERNITY HOSPITAL: PRELIMINARY REPORT

by

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The Victoria Jubilee Hospital in Jamaica is entirely devoted to obstetrics. It has 164 beds and provides 70 percent of the public (non-private) beds for a population of 430,000 in the largely urban and suburban areas of Kingston and St. Andrew.

Between January 1 and December 31, 1963, there were 14,299 deliveries in this hospital. There has always been a great demand by our patients for sterilization procedures, but because of staff shortages and extreme shortage of beds it is becoming increasingly difficult for us to do these operations on the grounds of multiparity. Even so, 131 sterilization operations were performed in 1963.

Our experience over the years had led us to believe that nothing short of total and irreversible contraception produced by sterilization was acceptable to women of high parity in the lower social and economic groups to which the majority of the hospital patients belong; and that other methods of contraception, where these have been tried, have been rejected because of recurrent cost, inconvenience, and difficulties of application.

It therefore came as a great surprise to us to learn that our patients were interested in a method of contraception other than sterilization. This was evident when a single sampling was made one morning of 34 patients who were about to be discharged from the puerperal wards of the hospital. They were individually asked this question: — "If there were a new method by which you could be stopped from having any more children *and which did not involve an operation*, would you be interested?" Of these 34 patients, 24 said *Yes*. The remaining 10 were either Para I, II, or III, or had experienced misfortune in an earlier pregnancy.

Accordingly a program of intra-uterine contraception was launched at the hospital on April 5, 1964, with a grant provided by The Population Council. It was decided to restrict the program to postpartum patients.

Information about this service had to be provided. We were however very anxious to avoid any appearance of forcing birth control upon our patients. Therefore, each morning our clinic nurse would visit the puerperal wards and in a general way tell the patients of our clinic facilities. A printed invitation to return to the hospital on any of three mornings to see the nurse and make an appointment for the clinic was then handed to those patients who indicated their interest. The response was disheartening. It seemed that the patients simply took the invitations away and forgot about them. Also a number of our patients were undoubtedly illiterate, and this problem became immediately obvious. In one month's trial we had only 30 patients. This approach was therefore abandoned. Thereafter the clinic nurse visited the wards each morning and gave to each interested patient a firm appointment to the clinic, thereby cutting out an unnecessary visit to the hospital. The response was overwhelming and in a very short time we had more patients than we could cope with.

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Clinics are held twice a week and each clinic is limited to 25 new patients. Between April 1 and August 31, 1964, 684 women attended for insertions.

Some of the social and economic characteristics of the 684 patients may be noted. Sixty-two percent were in the age range of 20 to 29 years. Twenty-one percent were legally married; the rest were either common-law partners or single women. Over two-thirds normally had paid employment. All but 3 percent had some primary education; the average period of schooling was 4.9 years. The 684 women had borne a total of 3,222 children; 60 percent had 3 to 5 living children. Two-thirds of the patients wished to have no more children, mostly because of economic difficulties. About 84 percent said neither they nor their husband or partner had ever used any contraceptive method.

A Lippes loop size 3 was used on all patients, and insertions were made any time after the sixth postpartum week; 55 percent of the patients had begun to menstruate again at the time of insertion. Papanicolaou smears were taken routinely; 284 of these have so far been reported: 270 were Class 1 and 14 were Class 2. In 684 insertions it was necessary to dilate the cervix in 37 patients. We were however disappointed at the number of times it was necessary to apply a vulsellum to the cervix because the inserter did not pass easily through the cervical canal but tended to push the uterus out of the pelvis.

We proposed in this study to follow our patients at three months, nine months and 21 months after insertion. Patients were however free to return to our clinic at any time if they had any problems. Table 1 shows an analysis of 88 patients who returned before their first follow-up visit was due.

TABLE 1

Reasons for returning before first scheduled follow-up

	No. of patients	% of 684 insertions
Expulsion	26	3.8
Irregular bleeding	18	2.6
Menorrhagia	12	1.8
Metrorrhagia	12	1.8
Pain	10	1.5
Discharge	6	0.9
Miscellaneous	3	0.4
Requesting removal	1	0.1
Total	88	12.9

There were 26 expulsions and in eight instances this occurred during a menstrual period. Not included among these is one patient who undoubtedly is pregnant; we are not sure whether the device is still in place, but are unwilling to expose her to X-ray examination at this stage. Bleeding is our biggest single problem, and this occurred in 52 patients. There were 18 patients with irregular bleeding; in half of these it dated from the time of insertion, and was severe enough in one patient to warrant removal. One patient had insertion six weeks after cesarean section; this was probably too early. In three patients there was associated abdominal pain.

One patient expelled the device during an episode of bleeding, and it was reinserted. Twelve patients complained of intermenstrual bleeding, which has settled down in all cases. One patient had an erosion and one had been receiving injections of a progestogen contraceptive agent prior to insertion.

Ten patients complained of abdominal pain; two of these requested removal of the device, and it was removed in one case. Another patient had undoubted evidence of acute pelvic infection and the device was removed. One patient complained of dyspareunia. Three patients had tenderness on pelvic examination and were treated as low-grade pelvic infections with antibiotics.

Six patients complained of vaginal discharge. Of these one patient had a cervical erosion and *Trichomonas vaginalis*, the others were of non-specific etiology. On the other hand we have found a number of patients with *Trichomonas vaginalis* who did not complain of discharge.

One patient requested that the thread be shortened, and two patients returned because they could not feel the thread on self-examination. The device was removed at the request of one patient with a vague complaint that she was not keeping health.

For the routine follow-up three months after insertion, 216 patients were seen up to the end of August 1964. Of these, 62.5 percent had no symptons.

TABLE II

Follow-up at 3 months after insertion

	No. of patients	Percent
No symptoms	135	62.5
Menorrhagia and other	23	10.6
Menorrhagia only	17	7.9
Dysmenorrhoea	16	7.4
Metrorrhagia	10	4.6
Expulsion	10	4.6
Pain	5	2.3
Total	216	100

Again bleeding has been our greatest problem—menorrhagia occurring in 18.5 percent with or without associated dysmenorrhea, metrorrhagia, or abdominal pain. In no case has it been necessary to remove the device because of bleeding or pain. Five patients had expelled the device prior to their follow-up examination. In four cases the device was found on examination to be lying in the vagina, and in one case it had been partially extruded through the external os. All expulsions were reinserted. No patient was found to be pregnant, but four were recorded as "doubtful pregnancy."

At this examination we were impressed at the high percentage (64) of women in whom the thread was not visible at speculum examination. We believe that this was due to cutting the thread too short in the early days of the study through an exaggerated concern for the sensitivity of the Jamaican male; we believe too that the gaping of the external os when the blades of the speculum are opened gives a false impression that a sufficient length of thread has been left behind. That it is insufficient becomes apparent at once when the blades of the speculum are closed prior to its removal and the lips of the cervix fall into apposition around the thread. We wonder, however, whether the device has not been misplaced in the uterine cavity in some of the patients in whom the thread is not visible. X-ray examination of one patient who complained of not feeling the thread, which she had felt the previous day, showed the device lying in the correct plane but upside down in the uterine cavity.

This program of intra-uterine contraception has been in progress for too short a time to evaluate its effectiveness. Acceptability is high among these patients, who had previously not practised contraception consistently, if at all, in spite of a desire to limit fertility. Re-examinations at nine monhts after insertion will take place early in 1965.

INTRA-UTERINE CONTRACEPTION WITH THE USE OF A FLEXIBLE NYLON RING: EXPERIENCE IN SANTIAGO DE CHILE

by

JAIME ZIPPER, M.D., M.L. GARCIA, M.D., and L.L. PASTENE, M.D.*

Our clinical experience in this field started in 1959, following the published reports of Ishihama[6] and Oppenheimer.[9] At the first conference on intra-uterine contraceptives[10] it was clearly stated that the possibility of widespread use of intra-uterine contraceptives suggested a promising method of regulating fertility. At that meeting all the facts then known, on the basis of the results obtained by several authors, were reviewed. Hall and Stone[5] described their experience with the stainless steel ring. Margulies[8] and Lippes[7] contributed strongly in this field with their renowned spirals and loops made of plastic material. On that occasion it was also demonstrated that the newest modifications of the Gräfenberg[4] ring proved to be safe and efficient. One such modification, consisting of a flexible ring of nylon with a tail, was developed by us and employed widely in a section of Santiago containing over 650,000 inhabitants.

At the obstetrical and gynecological service of the Barros Luco Hospital, which is situated in this area, 14,163 deliveries took place during 1963. In the same period 5,110 women were hospitalized for complications following illegal abortions. Our experience with intra-uterine devices, as reported to the 1962 meeting,[12] was based on 628 patients from a group of 1,252 who were fitted with the ring. Now, only two years later, 6,500 women have been fitted with the device. We shall describe the results obtained with the first 3,000 ring wearers during the period from October 1959 to June 1963.

Materials and methods

The device used is made of a thread of nylon about 2 m in length and 0.35 mm in diameter, coiled by hand into 20 interlaced rings, with a final diameter of 25 mm. About 200 mm of the end of the thread is left free; after insertion it extends about 30 mm into the vagina, providing a simple means of localization and extraction. If the tail does not extend into the vagina, as sometimes happens, location and removal are accomplished by the use of an intra-uterine hook. An aluminum rod, 3 mm diameter, with a groove at the end, is used as an inserter (Figure 1). Before insertion both ring and inserter are sterilized by immersion in an ethanol-iodine solution. Insertion is performed without dilation of the cervical canal. In our clinic insertions are performed by physicians and two experienced midwives following routine hysterometry.

Our patients were not selected by us, but came to us as applicants for medical attention at the hospital. Many of them were postpartum patients in the first 50 days after delivery; others came from the Department of Gynecology 40 days after curettage was performed as a consequence of illegal abortion, mostly under septic conditions. The sole indication for

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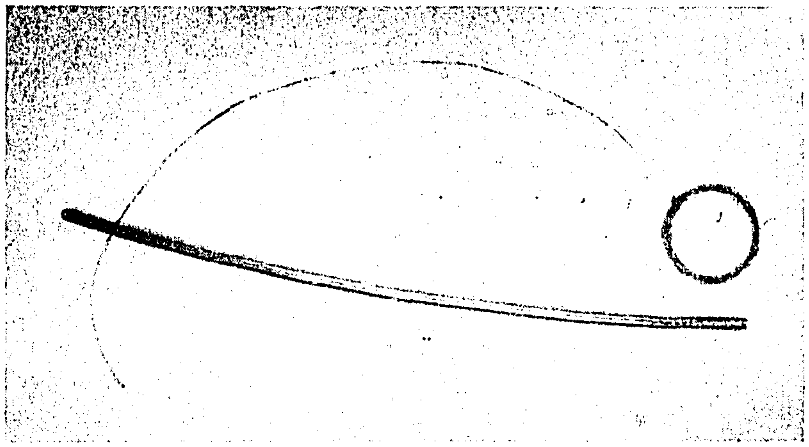

Fig. 1. Intra-uterine contraceptive device of nylon thread, and aluminum rod used as inserter.

exclusion of any patient was the presence of severe signs or symptoms of gynecological diseases, especially chronic adnexitis. Insertions were made in the presence of both cervicitis and vaginitis. No serious difficulties arose during insertion. In three instances the uterus was perforated by the hysterometer before the insertion; no complications from these perforations were registered. In spite of the fact that the insertion usually was made either immediately after the menses or 40 to 50 days postpartum, the ring was inadvertently inserted in a pregnant uterus in 11 cases.

Among the 3,000 patients fitted with the device, the 709 insertions in the first year may be regarded as a special group, because several designs made of polyethylene and nylon materials were tried before we adopted one design for regular use. This group of 709 experimental ring insertions is thus treated separately in the analysis of our results.

Results

Among the 3,000 cases under study, 667 (22.2 percent) were closed because of expulsion, removal, or pregnancy; 635 were lost to follow-up. The remaining 1,698 cases were regularly followed up until June 30, 1964. Follow-up examinations were scheduled at intervals of not more than 6 months, and cases were classified as "lost to follow-up" when they were at least 3 months overdue for a scheduled examination. Table I* shows the duration of use of all cases, active and closed.

The experimental group, consisting of the first 709 insertions, experienced a total of 14,038 woman-months of use. Because of the experimental nature of the device used and the large number of cases lost to follow-up, actually only 129 (18.2 percent) of this group are active cases. In the regular group, containing 2,291 women with a total experience of 35,606 woman-months of use, 1569 (68.7 percent) are active cases (Table II).

The relevant clinical facts encountered were classified as follows: (1) expulsions, (2) removals for medical reasons, (3) removals for non-relevant reasons, and (4) pregnancies.

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* The authors gratefully acknowledge the assistance of the National Committee on Maternal Health, New York City, and its research director, Dr. Christopher Tietze, who analyzed our data and prepared the tables presented at the end of this paper.

1. *Expulsions.* Table IX shows both expulsions and medical removals by parity. The cumulative rate of expulsion per 100 cases during the first year after insertion is 17.2; the rate decreases in inverse relation to parity. Table VIII shows the number of reinsertions and repeated expulsions. The rate of repeated expulsion after one previous expulsion is 26.8. Thus the initial rate of expulsion of 17.2 is decreased to 4.6 by re-insertion. In Table VII, first expulsions are classified as "noticed" and "not noticed." Of 495 expulsions, 249 or only about half were noticed by the patient.

2. *Removals for medical reasons.* Table V includes all first removals, whether for medical or personal reasons. The total rate of removal of the experimental ring for medical reasons is 7.9 percent (99 cases); of the regular ring 5.7 percent (138 cases) were removed. We instituted estrogenic treatment for metrorrhagia during the first month after insertion of the regular rings; the decreased rate of removal of regular rings is attributed to this treatment.

In Table IX the removals for medical reasons are grouped by parity. The final rate of removal for all 3,000 cases in the first year was 6.3 percent.

Medical reasons for removal of the device included bleeding, pain, infection, cervicitis, psychiatric reasons, and pregnancy at insertion, as shown in Table VII. Bleeding was the most frequent cause of removal, and includes all the cases of menorrhagia, polymenorrhea, or metrorrhagia following the first insertion. Staining or spotting during the first ten days was not included, unless the case required special treatment. There were 154 cases of irregular bleeding registered (6.5 percent); in 129 of these cases (5.4 percent) removal of the ring was indicated. Pain was a rather infrequent symptom; only 18 removals were made for this reason. Infection appeared in 31 cases; this will be discussed later, along with other complications attributed to the method. Removal was indicated in 25 cases of cervicitis, and in 11 cases of inadvertent insertion into a pregnant uterus.

In 209 cases, the ring was removed temporarily for treatment of cervicitis or to perform biopsies, or simply to change to another device. Among these 209 patients in whom the ring was replaced after removal there have been only 26 expulsions (12.4 percent). This rate is less than half the rate of expulsions following replacement of expelled rings.

3. *Removals for non-relevant reasons.* As shown in Table VII, 92 removals were made for personal reasons, which were mostly related to fear, especially of infection and cancer. The rate of such removals is lower with the regular than with the experimental ring.

4. *Pregnancies.* As shown in Table VII, of a total of 155 unintended pregnancies, 69 occurred with the device *in situ*, and 85 were undetermined. Tables III and IV present an analysis of unintended pregnancies, and Table VI shows monthly pregnancy rates by period since insertion.

Comments

The data and observations reported here undoubtedly indicate that we have a technique of great value for the safe control of mass population growth. It is true that some aspects of the technique may be controversial or may require further comment. These are discussed in the following paragraphs.

Acceptance. Many factors are involved in the acceptance of a method. It depends largely upon the physician, the patient, and on the rules governing the practice of medicine in a given country. These contribute fundamentally to the usefulness or uselessness of any method. We believe that the so-called "cafeteria choice" is not advisable—in our opinion the medical profession rather than the patient must ultimately decide on the efficiency of any procedure in the light of all the relevant factors, and accommodate one or several techniques to the specific conditions of a country.

In many countries very low clinical effectiveness has been reported for the traditional contraceptive methods,[3] which seem to require a relatively high level of motivation in order to be effective. Therefore we think that mass application of such methods is not advisable from an economic and demographic point of view.

The method used by us has been widely accepted in Chile, especially in the medical field[2] and by the National Public Health Service. Another factor of great importance is the low cost of our technique, which makes it applicable to all economic levels in the population.

Finally, we feel that the most adequate indicator for a real appraisal of the utility of a method is the level of uninterrupted use. Thus in our studies the percentage of women still using the ring, without having conceived and without complication, was close to 70 percent, with an average of 16.6 months of use per woman, and a total exposure of 49,644 months.

Complications may be divided into two groups, those occurring as a direct consequence of insertion, and conditions which may or may not be attributed to continued use of the method. The complications occurring as a direct consequence of insertion include metrorrhagia and expulsion of the device. As already described by other authors, metrorrhagia is the most troublesome side effect, but we feel that it is functional in character. We found metrorrhagia to be significantly reduced by estrogenic treatment, especially in the first month. Of the 56 cases of metrorrhagia that required removal of the ring, 41 (73.2 percent) occurred in the first 1,000 cases, before the use of estrogens was begun.

In our study, expulsion was the major cause for discontinuation of the method, largely because 125 cases from the first 468 expulsions were not reinserted. First expulsions of the nylon ring reached 17.2 per 100 insertions in the first year. Devices with lower rates of expulsion, as reported by C. Tietze at this conference, are the large loop (9.0 percent), the steel ring (8.7 percent) and the plastic bow (3.8 percent), used by other investigators. Reinsertion of the nylon ring increases the retention rate considerably—the expulsion rate was lowered from 17.2 to 4.6 when expelled devices were reinserted.

The problem of expulsion has been one of the major interests of those who have worked on the improvement of the device and of the general technique. We feel that the initial expulsion is due to various factors, such as uterine adaptation, uterine irritability, and the elasticity of the ring. All the new devices used are based upon the principle of introducing an elastic foreign body into the uterine cavity. The elasticity permits easy insertion, but also facilitates expulsion. If the device were modified so as to have a rigid body, articulated to permit easy insertion, it is expected that the expulsion rate would diminish, although other complications might increase. Figure 2 illustrates one possible modification along these lines; it is only a rough draft.

The complications that may be attributed to use of the method include cancer and infection. Two cases of cervical cancer were diagnosed among the 6,500 women who have been fitted with rings at Barros Luco Hospital. One of these is among the 3,000 cases analyzed in this study; diagnosis was made at the time of routine examination. An analysis of the frequency of neoplasia appearing in our group reveals no difference from those encountered in control groups of our gynecological clinic. The strict evaluation of any influence this technique may have on the incidence of gynecological cancer requires a long-term study of a much larger sample.

Of the 31 cases of infection recorded, 10 were diagnosed as endometritis and 21 as pelvic inflammatory disease (PID). Of the latter, 13 did not require hospitalization but received antibiotic treatment; the remaining 8 patients were hospitalized. Three PID cases occurred

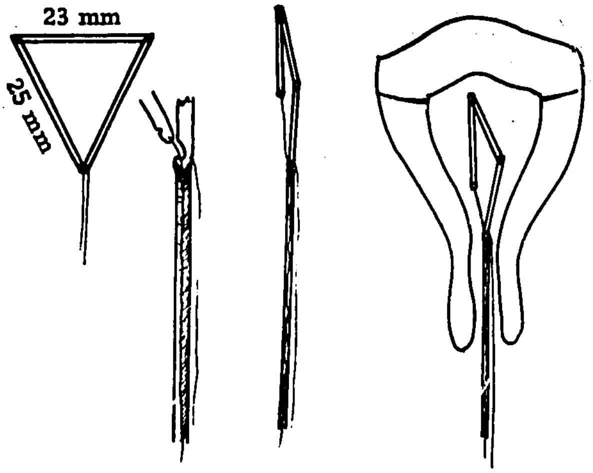

Fig. 2. Sketch of articulated intra-uterine contraceptive device, designed to combine rigidity *in situ* with ease of insertion.

in the first month after insertion, but only one of these required hospitalization. It is at present difficult to determine whether this side effect was induced by the ring or whether it appeared because of aggravation of a chronic condition. Our belief is that a slight aggravation of chronic pelvic inflammation might well be the sole risk in the use of intra-uterine contraceptives.

Despite this risk, it seems worth while to employ the method, especially if it enables us to reduce the rate of increase of the population with a penalty of only 8 hospitalizations in 4,130 woman-years of use. This means that in our district, with 120,000 fertile women, a maximum of 232 hospitalizations for PID could be expected during the first year, assuming that all women used the ring. When this figure is compared with the 5,110 hospitalizations that occur annually because of illegal abortions, the merits of the method become clear.

Unintended pregnancies. The most astonishing fact about this technique is that only 1.69 pregnancies occurred per 100 years of exposure with the ring *in situ*; when pregnancies with ring undetermined are included, the rate is 3.75—still an exceedingly low failure rate. As mentioned earlier, 41.0 percent of the pregnancies occurred within the first 3 months after insertion when expulsions are at their maximum. It is our impression that many of the pregnancies with device undetermined occurred in fact without the device in place.

Among all 155 contraceptive failures, one unintended pregnancy was ectopic. In this respect, our observations confirm those of Tietze[11] on the low incidence of tubal pregnancies in ring wearers. This may be a clue to some aspects of the mechanism whereby the device exerts its contraceptive effect. (See the report on our experiments with laboratory animals, page 198.)

Restoration of fertility following ring removal. In 12 cases the ring was removed at the request of women who wished to become pregnant. In the follow-up of these cases, 7 reported conception within the first month, 1 in the second month, and 1 during the third month. The remaining 2 have not as yet become pregnant, although their rings were extracted in March and May, 1964. Only one woman was lost to follow-up. All the pregnancies developed normally, and there have been 4 successful deliveries so far.

Demographic implications. We agree with the conclusions of Berelson and Freedman[1] concerning their studies in Taiwan. The success of their program appears to depend on the use of intra-uterine contraception; despite the "cafeteria choice" offered to acceptors, 78 percent of them chose IUCD. The rate of continued use that we found comes close to that observed in Taiwan.

Nevertheless, there is one serious obstacle that will, we think, decrease the demographic efficiency of this method: its widespread application depends on the use of physicians in a well-coordinated cooperative medical program. In Chile, after intra-uterine contraception started to be widely employed in 1964, a large number of contraceptive clinics have been created, financed and supported by the National Public Health Service, with a theoretical capacity of 30,000 insertions a year in Santiago. These clinics, as time goes on, are becoming more and more involved in other activities, becoming in fact centers for the early diagnosis of cancer, treatment of vaginitis and cervicitis, etc. Although the level of hygiene and health will thereby be improved, the clinics are not as effective as they might be in lowering the birth rate. Nevertheless, despite the complexities of an experimental program of population control, or of a campaign to replace illegal abortion by a preventive technique, we are convinced that intra-uterine contraception is the only method known that offers hope in the developing countries.

Conclusions. Gräfenberg's technique has been shown to have a failure rate of only 3.75 per 100 woman-years of exposure. There is a high level (71.6 percent) of continued use of the device. Removal of the device restores fertility when pregnancy is desired. The minor complications encountered among ring users do not increase the risks now accepted as normal in obstetrical and gynecological practice.

Compared with the intra-uterine devices used by other investigators, such as the larger loops and the stainless steel ring, the nylon device used in our investigations has the following characteristics:

1. A relatively high rate of first expulsions (17.2%).
2. A low rate of repeated expulsions (26.8%), which lowers the over-all expulsion rate to 4.6%.
3. A very low rate of removal for medical reasons with the regular ring (5.7%).
4. Extreme simplicity and cheapness, which permits any physician or clinic interested in contraception to use this highly effective technique, even if no resources are available.

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TABLES: BARROS LUCO HOSPITAL STUDY

by

CHRISTOPHER TIETZE, M.D.

TABLE I

Total, active and closed cases by duration of use

Duration of use (months)	Total cases	Active cases	Closed cases*
0–1	432	—	432
1–2	99	—	99
2–3	69	—	69
3–6	188	—	188
6–9	117	—	117
9–12	90	—	90
12–18	761	629	132
18–24	592	514	78
24–36	332	260	72
36–48	257	235	22
48–60	63	60	3
Total	3,000	1,698	1,302

* Including 635 cases lost to follow-up.

TABLE II

First insertions, total insertions, active cases, and aggregate woman-months of use, by type of ring

Type of ring	First insertions	Total insertions	Active cases	Woman-months of use
Experimental	709	768	129	14,038
Regular	2,291	2,901	1,569	35,606
Total	3,000	3,669	1,698	49,644

TABLE III

Unintended pregnancies, reported and hypothetical, by type of ring: numbers and rates

	Reported pregnancies		Hypothetical pregnancies*	
Type of ring	Number	Rate	Number	Rate
Experimental	45	4.9 ± 1.0	96	9.2 ± 1.3
Regular	110	4.4 ± 0.5	306	12.0 ± 0.8
Total	155	4.5 ± 0.5**	402	11.3 ± 0.7

* Assuming no routine visits and all unnoticed expulsions followed by conception. Number of hypothetical pregnancies equals reported pregnancies plus unnoticed expulsions.

** Rates computed according to the life table procedure described by Robert G. Potter (*Milbank Memorial Fund Quarterly*, 41: 400-418, Oct. 1963).

TABLE IV

First expulsions, excluding and including pregnancies with device undetermined, by type of ring: numbers and rates

	Excluding pregnancies		Including pregnancies	
Type of ring	Number	Rate	Number	Rate
Experimental	111	14.7 ± 1.5	135	17.4 ± 1.6
Regular	384	18.0 ± 0.9	445	20.3 ± 0.9
Total	495	17.2 ± 0.8	580	19.6 ± 0.8

TABLE V

First removals for medical and personal reasons, by type of ring: numbers and rates

	Medical reasons		Personal reasons	
Type of ring	Number	Rate	Number	Rate
Experimental	99	7.9 ± 1.1	45	2.9 ± 0.8
Regular	138	5.7 ± 0.6	47	1.8 ± 0.3
Total	237	6.3 ± 0.6	92	2.1 ± 0.3

TABLE VI

Monthly rates of pregnancies, expulsions, removals for medical reasons, and loss to follow-up, by period since insertion

Period since insertion (months)	Pregnancies	Expulsions	Removals (medical)	Loss to follow-up
0–1	0.1	7.3	2.4	11.0
1–2	0.6	3.0	0.6	1.0
2–3	0.5	2.0	0.3	1.2
3–6	0.5	0.8	0.4	1.3
6–9	0.4	0.9	0.3	0.8
9–12	0.2	0.4	0.4	0.5
12–18	0.2	0.2	0.2	0.5
18–24	0.1	0.3	0.5	0.5
24–36	0.2	0.2	0.4	0.5
36–48	0.1	0.1	0.3	0.1

TABLE VII

Unintended pregnancies, first expulsions, and first removals for medical and personal reasons, by specific categories and type of ring

	Experimental	Regular	Total
Unintended pregnancies			
Device *in situ*	21	48	69
Device *in situ* — ectopic	—	1	1
Device undetermined	24	61	85
	45	110	155
Expulsions			
Noticed — complete	61	187	248
Noticed — incomplete	—	1	1
Not noticed — complete	32	78	110
Not noticed — incomplete	18	118	136
	111	384	495
Removals for medical reasons			
Bleeding	56	73	129
Pain or discomfort	7	11	18
Infection	8	23	31
Cervicitis	13	12	25
Psychiatric	2		2
Pregnant at insertion	2	9	11
Other	11	10	21
	99	138	237
Removals for personal reasons			
Fear	15	13	28
Husband's objection	—	1	1
Patient's request	30	33	63
	45	47	92

TABLE VIII

Reinsertions and repeated expulsions

Number of previous expulsions	Number of reinsertions	Repeated expulsions	
		Number	Rate*
One	343	82	26.8 ± 2.6
Two or more	50	13	30.7 ± 7.1
One or more	393	95	27.2 ± 2.4

* Cumulative rate per 100 insertions during first year after insertion.

TABLE IX

Expulsions and removals for medical reasons, by parity

Parity	Number of cases	Expulsions		Removals	
		Number	Rate*	Number	Rate*
0	2	—	NC	1	NC
1	63	13	NC	3	NC
2	287	69	26.4 ± 2.9	23	8.5 ± 2.0
3	617	110	18.9 ± 1.7	39	6.3 ± 1.1
4 or 5	1044	161	16.8 ± 1.2	83	6.7 ± 0.9
6 or 7	545	72	14.0 ± 1.6	38	6.0 ± 1.8
8 or more	397	38	10.1 ± 1.6	19	3.7 ± 1.1
NS	45	5	NC	1	NC
	3,000	468	17.2 ± 0.8	207	6.3 ± 0.5

NS = Not stated NC = Not computed

* Cumulative rate per 100 cases during first year after insertion.

INTRA-UTERINE CONTRACEPTION: EFFECTIVENESS AND ACCEPTABILITY

by

CHRISTOPHER TIETZE, M.D. and SARAH LEWIT*

This report covers the first year of a cooperative statistical program, undertaken by the National Committee on Maternal Health (NCMH) as part of a comprehensive investigation of intra-uterine contraceptive devices (IUCD), sponsored by The Population Council.The report is based on the records submitted through June 30, 1964, by 38 participating institutions and investigators in private practice; all but 4 of these are located in the United States, including one in Puerto Rico.

The number of cases, both active and closed, and the aggregate woman-months of use for each investigator are shown in Table I. Although the program is barely a year old, the experience shown for some investigators extends over a much longer period because retrospective data were included. As of June 30, 1964, the total number of patients or cases for all investigators combined was 16,734, of which 13,305 were active and 3,429 closed. For all cases, both active and closed, the aggregate period of use totalled 132,460 woman-months.

Table II shows the numbers of total, active, and closed cases by duration of use since first insertion. Owing to the rapid expansion of the program, only 43 percent of all women had worn an IUCD for six months or more and 21 percent for one year or more. The corresponding figures for active cases were 45 percent and 23 percent, respectively.

Table III summarizes the numbers of first insertions, total insertions, active cases, and aggregate woman-months of use for each of six types of IUCD and a residual group comprising the remaining devices, most of which have been under study for less than six months. The six devices shown separately are those with at least 4,000 woman-months of use. These are: the Margulies spiral and the Lippes loop (each in two sizes, identified as "large" and "small" in this report), the plastic bow of Birnberg (size 3), and the stainless steel ring of Hall and Stone (Figure 1).[1-4] For each device, the difference between first insertions and total insertions represents the number of second and subsequent insertions following pregnancies, expulsions, or removals. For all devices combined, there were 2,593 reinsertions.

Although, at the time of their introduction, the small spiral (size 5-J) and loop (size 1) and the size 3 plastic bow were used generally, their insertion is currently restricted to nulliparous women. Data for the large spirals (size 5) and loops (size 2) appear in this report; for the large bow (size 5), which is currently being tested, available data are too limited for statistical analysis.

Among the 16,734 patients covered in this report, 278 experienced an *unintended pregnancy*, i.e., a conception after insertion of the IUCD and prior to a removal or an expulsion noticed by the woman. The term includes pregnancies for which the position of the device at the time of conception was undetermined. The first two columns of Table IV show, for each

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* National Committee on Maternal Health, Inc., New York, New York.

TABLE I

Total cases, active cases, closed cases, and aggregate woman-months of use, by institution or investigator

Institution or investigator	Total cases	Active cases	Closed cases	Months of use
Mount Sinai Hospital, N.Y.C.	2,168	1,601	567	18,659
Buffalo Planned Parenthood Center	1,949	1,471	478	21,054
College of Physicians & Surgeons, N.Y.C.	1,474	1,311	163	8,951
Ryder Memorial Hospital, Humacao, P.R.	1,160	720	440	12,970
Hong Kong Family Planning Ass'n	1,000	945	55	2,839
Temple University, Philadelphia	960	650	310	6,831
Obst. Gyn. Group, Perth Amboy, N.J.	795	529	266	12,551
Albert Einstein Medical College, Bronx	722	665	57	2,690
Margaret Sanger Research Bureau, N.Y.C.	610	420	190	4,853
N.C. State Board of Health, Raleigh	494	402	92	1,955
Rochester Planned Parenthood Center	483	424	59	1,400
University of Michigan, Ann Arbor	445	367	78	2,082
San Francisco Planned Parenthood Ass'n	361	303	58	1,750
Dr. Jack Lippes, Buffalo	319	222	97	4,996
Dr. Lazar C. Margulies, N.Y.C.	319	251	68	3,835
Medical Department, Suva, Fiji	282	269	13	671
Los Angeles Planned Parenthood Centers	268	227	41	1,104
Dr. Herbert Hall, N.Y.C.	243	181	62	9,130
New York University	243	195	48	1,553
Dr. Marvin B. Zuckerman, N.Y.C.	217	192	25	4,705
Pennsylvania Hospital, Philadelphia	202	190	12	545
Cornell Medical Center, N.Y.C.	166	161	5	324
Metropolitan Hospital, N.Y.C.	163	155	8	318
New York Medical College	160	129	31	802
Mecklenburg County Health Dept., N.C.	160	154	6	342
Lenox Hill Hospital, N.Y.C.	157	144	13	786
National Ass'n for Sex Education, Stockholm	151	144	7	472
Dr. Charles C. Bollinger, Gallup, N.M.	150	119	31	492
Dr. Charles H. Birnberg, Brooklyn	138	111	27	945
Cleveland Maternal Health Ass'n	136	112	24	408
Chicago Planned Parenthood Ass'n	133	122	11	351
Dr. Herbert W. Horne, Boston	98	63	35	590
Devon & Cornwall Clinics, England	95	95	—	289
University of Oregon, Portland	82	77	5	166
Brookdale Hospital, Brooklyn	75	69	6	263
Ohio State University, Columbus	61	46	15	148
Dr. Martin L. Stone, N.Y.C.	56	32	24	562
Henry Ford Hospital, Detroit	39	37	2	78
Total	16,734	13,305	3,429	132,460

major type of IUCD, the number of patients who experienced pregnancy and the cumulative pregnancy rate per 100 cases during the first 12 months after insertion. These rates* were computed according to the life table procedure recently described by Robert G. Potter.[5]

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* Because many patients have experienced more than one insertion of the same type or of different types of IUCD, the information reported to NCMH is coded and tabulated in terms of *segments.* A segment is defined as a period of use beginning with an insertion and either continuing or

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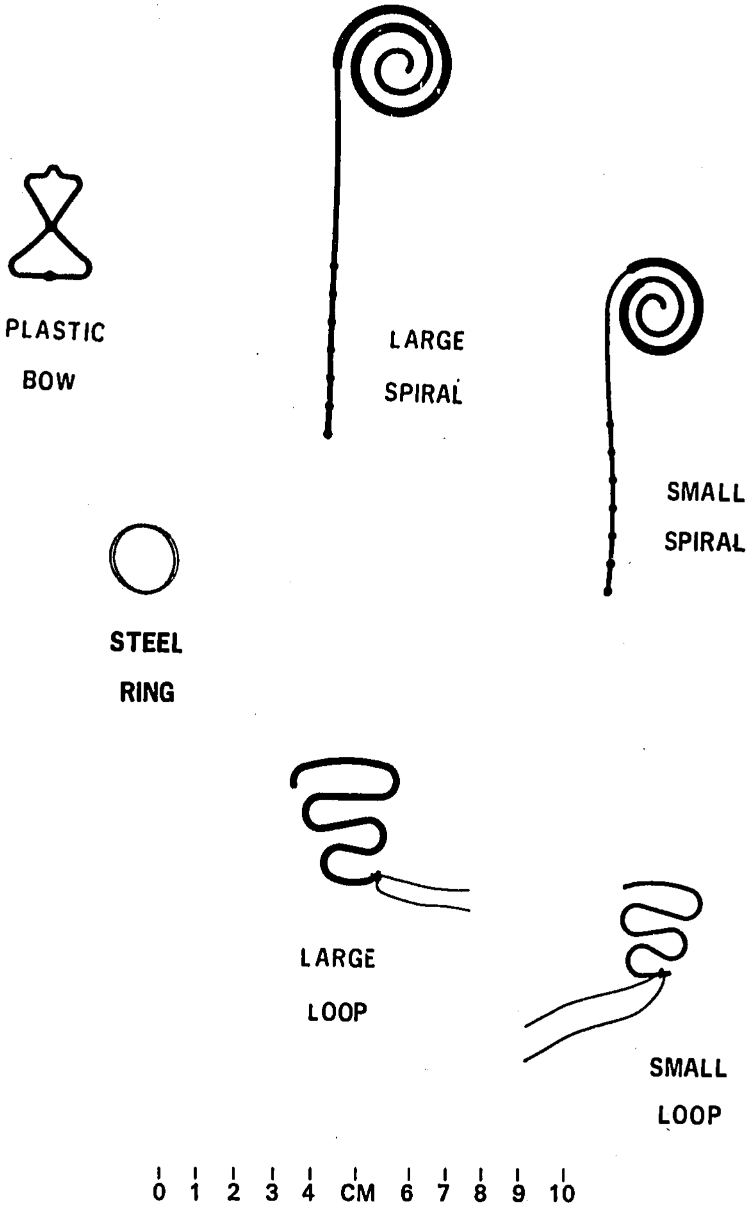

Fig. 1. Principal types of intra-uterine contraceptive devices investigated in the cooperative statistical program. The scale represents centimeters.

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terminated by pregnancy, expulsion, or removal of the device, or lost to follow-up without removal of the IUCD. All monthly and cumulative rates shown in this report, with the exception of the expulsion rates in Table VII, and the rate of planned pregnancies in Table X, are based on experience during first segments only, a procedure involving fewer tabulations, and therefore less expensive than any one of several alternate approaches. The results differ only minimally from those computed by other methods.

TABLE II

Total cases, active cases, and closed cases, by duration of use

Duration of use (months)	Total cases	Active cases	Closed cases
0–3	5,758	4,121	1,637
3–6	3,819	3,218	601
6–9	2,036	1,619	417
9–12	1,526	1,283	243
12–18	1,690	1,374	316
18–24	928	800	128
24–36	753	691	62
36–180	224	199	25
Total	16,734	13,305	3,429

TABLE III

First insertions, total insertions, active cases, and aggregate woman-months of use, by type of device

Type of device	First insertions	Total insertions	Active cases	Months of use
Large spiral	4,044	4,613	2,689	33,467
Small spiral	786	996	423	8,103
Large loop	4,100	4,770	3,814	27,772
Small loop	931	1,060	279	10,855
Plastic bow	1,606	1,750	1,527	7,899
Steel ring	1,880	2,073	1,423	29,340
Other devices	3,387	4,065	3,150	15,024
Total	16,734	19,327	13,305	132,460

TABLE IV

Unintended pregnancies, reported and hypothetical, by type of device: numbers and rates

Type of device	Reported pregnancies		Hypothetical pregnancies	
	Number	Rate*	Number	Rate*
Large spiral	35	1.1 ± 0.2	102	2.9 ± 0.4
Small spiral	16	3.0 ± 0.8	35	5.5 ± 1.0
Large loop	33	1.3 ± 0.3	97	3.3 ± 0.4
Small loop	57	5.5 ± 1.0	120	11.4 ± 1.3
Plastic bow	47	5.5 ± 1.2	51	6.5 ± 1.4
Steel ring	59	3.6 ± 0.5	113	6.2 ± 0.7
Other devices	31	2.3 ± 0.7	98	5.0 ± 0.8
Total	278	2.6 ± 0.2	616	5.0 ± 0.3

* Cumulative rate per 100 cases during first year after insertion, with standard error.

The expulsion of an IUCD, if not noticed by the wearer, is usually soon followed by conception. Frequent pelvic examinations increase the chances of discovering an expulsion, and thus tend to reduce the incidence of pregnancy after expulsion. The third and fourth columns of Table IV show the hypothetical number and rate of pregnancies with all unnoticed expulsions added to the reported number of pregnancies on the assumption that *no* routine examinations were made and that *all* first expulsions not noticed by the wearer were followed by conception. Since the incidence of expulsions tends to decline with the passage of time, hypothetical pregnancy rates for the second and later years will be lower than those for the first year shown in Table IV. For the large spiral, the rate during the second year is estimated as 2.2 per 100 patients, and for the steel ring, as 2.4; rates for the other devices cannot as yet be computed.

Of the 278 unintended pregnancies reported, 149 occurred with the device known to have been *in situ* at the time of conception. The remaining 129 pregnancies were classified as "device undetermined." The designation "pregnancy after unnoticed expulsion" has not been used because the date of conception, as related to the date of expulsion of a device not *in situ*, can never be determined precisely. Examination after conception can reveal only whether the device is still *in situ*. The numbers and percent of pregnancies with device *in situ* and device undetermined, by type of device, appear in Table V. The proportions of pregnancies with device *in situ* and device undetermined for the small spiral and the steel ring, but not for the other devices, differ significantly from the corresponding proportions for all devices. In the case of the tailed devices, i.e., the spirals and loops, the presence of the IUCD can ordinarily be established by inspection or palpation. For these types of devices, the great majority of pregnancies with device undetermined are almost certainly pregnancies after unnoticed expulsion. The plastic bow and the stainless steel ring have no appendages and, therefore, cannot be seen or palpated. The presence of these devices can be ascertained only by probing the uterus or by X-ray—procedures which a clinician does not undertake during the early stages of pregnancy—or else in the course of a dilatation and curettage or at delivery.

TABLE V

Unintended pregnancies by location of device, by type of device: numbers and percent

Type of device	Device *in situ*		Device undetermined	
	Number	Percent*	Number	Percent*
Large spiral	21	60.0	14	40.0
Small spiral	13	81.2	3	18.8
Large loop	17	51.5	16	48.5
Small loop	34	59.6	23	40.4
Plastic bow	28	59.6	19	40.4
Steel ring	22	37.3	37	62.7
Other devices	14	45.2	17	54.8
Total	149	53.6	129	46.4

* Per 100 unintended pregnancies with device listed in stub.

Seven of the 149 unintended pregnancies with the device *in situ*, or one in 21, were ectopic. While the incidence of ectopic gestation is very high in relation to the number of pregnancies, it is very low in relation to the number of patients and to the length of time they have been under observation. As has been shown elsewhere,[6] interference with uterine implantation, assuming a normal rate of fertilization and a low rate of tubal implantation among the fertilized ova, would result in 8-12 ectopic pregnancies per 1,000 women per year. With 132,460 woman-months of observation, between 88 and 132 ectopic pregnancies could be expected, but only 7 were reported. These findings suggest that the contraceptive action of the IUCD involves factors other than interference with uterine implantation.

Expulsions include complete expulsions into or from the vagina and partial expulsions requiring removal from the cervix, whether noticed or unnoticed by the patient. While the number of unnoticed expulsions followed by pregnancies cannot be accurately established, the reported number of pregnancies with device undetermined provides an acceptable substitute. As shown in the first column of Table VI, the number of first expulsions, or the number of patients experiencing at least one expulsion, was 1,585, and the cumulative rate per 100 cases for the first year of use was 13.8. The estimated total number of expulsions, including 129 pregnancies with device undetermined, was 1,714 and the corresponding expulsion rate, 14.7 per 100 cases. Expulsion rates, as well as pregnancy rates, for the large spiral and loop were substantially lower than the corresponding rates for the smaller sizes. Because of the difficulty of determining the presence or absence of a tailless device, it is likely that the number of expulsions reported for these devices is too low, and the number of expulsions including pregnancies with device undetermined, too high.

TABLE VI

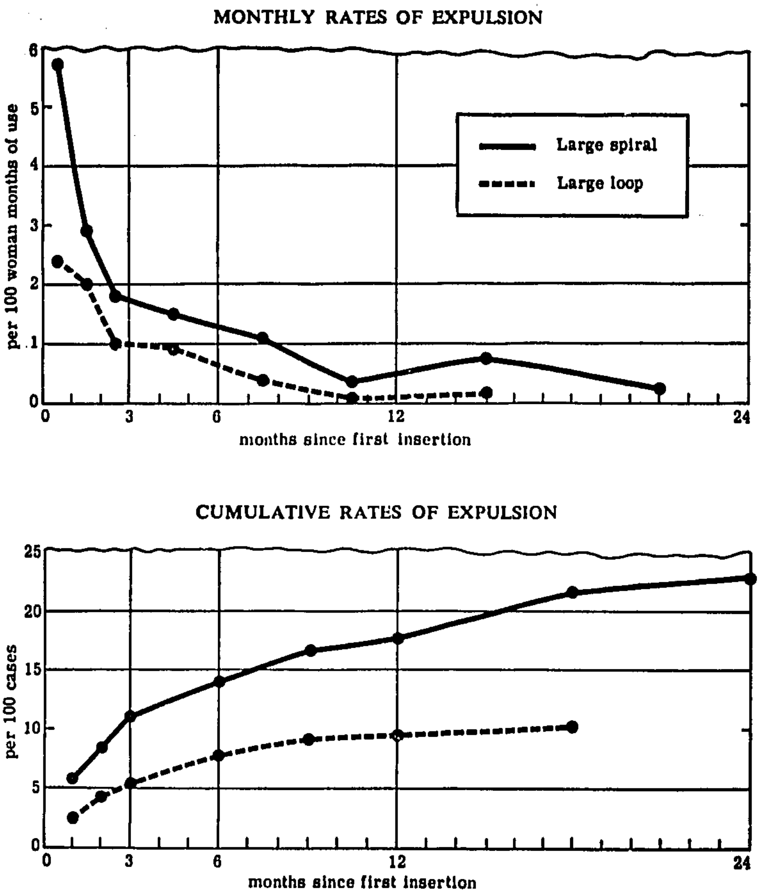
First expulsions, excluding and including pregnancies with device undetermined, by type of device: numbers and rates

Type of device	Excluding pregnancies		Including pregnancies	
	Number	Rate*	Number	Rate*
Large spiral	559	17.6 ± 0.7	573	17.9 ± 0.8
Small spiral	195	30.0 ± 1.9	198	30.2 ± 1.9
Large loop	241	9.0 ± 0.6	257	9.5 ± 0.6
Small loop	182	22.1 ± 1.6	205	24.0 ± 1.6
Plastic bow	22	3.8 ± 1.3	41	7.3 ± 1.8
Steel ring	143	8.7 ± 0.8	180	10.8 ± 0.8
Other devices	243	12.8 ± 1.0	260	13.6 ± 1.0
Total	1,585	13.8 ± 0.4	1,714	14.7 ± 0.4

* Cumulative rate per 100 cases during first year after insertion, with standard error.

Figure 2 shows monthly and cumulative expulsion rates for the two devices used most frequently in this study. The monthly rates are computed per 100 woman-months of use, and the cumulative rates per 100 cases. The horizontal time scale refers to the duration of use since first insertion. For both devices, the rates are carried forward to a point determined by the availability of an adequate number of cases. The monthly expulsion rates decline from a maximum during the first month after insertion to quite low levels in the later months. Correspondingly, the cumulative rates rise steeply during the early months, but very gradually during later periods.

Table VII shows the numbers and rates of unnoticed expulsions, excluding and including pregnancies with device undetermined. Of the 1,585 expulsions shown in the first column of Table VI, 1,247, or 4 out of 5, were noticed by the wearer and 338, or 1 out of 5, occurred without being noticed. As shown in the last two columns of Table VII, both the number and



MONTHLY RATES OF EXPULSION

CUMULATIVE RATES OF EXPULSION

Fig. 2. Monthly and cumulative expulsion rates for the large spiral and large loop.

TABLE VII

Unnoticed expulsions, excluding and including pregnancies with device undetermined, by type of device: numbers and percent

Type of device	Excluding pregnancies		Including pregnancies	
	Number	Percent*	Number	Percent*
Large spiral	67	12.0	81	14.1
Small spiral	19	9.7	22	11.1
Large loop	64	26.6	80	31.1
Small loop	63	34.6	86	42.0
Plastic bow	4	18.2	23	56.1
Steel ring	54	37.8	91	50.6
Other devices	67	27.6	84	32.3
	338	21.3	467	27.2

* Per 100 first expulsions of device listed in stub.

percentage of unnoticed expulsions increase—substantially in some instances—when 129 pregnancies with device undetermined are included with the expulsions.

Of the 1,585 nonpregnant patients experiencing an expulsion, 366 cases were closed; in other words, no device was reinserted. In the remaining 1,219 cases the first expulsion was followed by reinsertion of the same or another type of IUCD. A total of 398 patients experienced two or more expulsions: 282 had two each; 78 had three each; 20 had four each; and 18 had five or more expulsions apiece. One woman was willing to try again after 12 expulsions. The total number of reinsertions after one or more expulsions was 1,673, and the number of re-expulsions was 599. With all types of devices, expulsion rates were higher—much higher in most cases—after reinsertion than after first insertion, as can be seen by comparing Table VIII with Table VI. Moreover, the rates tended to be higher after two or more previous expulsions than after a single previous expulsion.

The number of patients who experienced a removal of the IUCD for medical or personal reasons were 1,248 and 222, respectively. Table IX shows these totals distributed by type of device, as well as cumulative removal rates per 100 cases during the first year.

TABLE VIII

Reinsertions after expulsion and repeated expulsions, by type of device: numbers and rates

Type of device	Number of reinsertions	Repeated expulsions	
		Number	Rate*
Large spiral	456	203	61.0 ± 2.9
Small spiral	162	91	74.3 ± 4.1
Large loop	291	79	37.4 ± 3.5
Small loop	69	41	68.7 ± 6.2
Plastic bow	95	5	7.3 ± 3.4
Steel ring	128	38	43.6 ± 6.3
Other devices	472	142	50.4 ± 4.6
Total	1,673	599	52.9 ± 1.7

* Cumulative rate per 100 reinsertions during first year after insertion, with standard error.

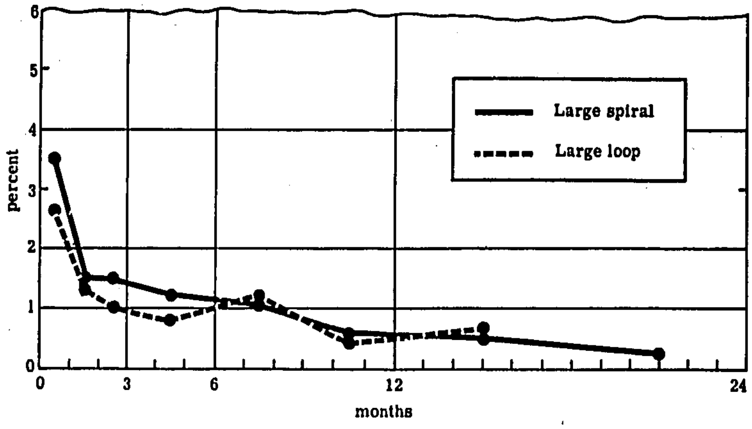
TABLE IX

Removals for medical or personal reasons, by type of device: numbers and rates

Type of device	Medical reasons		Personal reasons	
	Number	Rate*	Number	Rate*
Large spiral	435	14.2 ± 0.7	70	2.1 ± 0.3
Small spiral	79	11.9 ± 1.5	27	4.3 ± 1.0
Large loop	289	11.8 ± 0.8	38	2.3 ± 0.5
Small loop	147	13.3 ± 1.4	26	2.8 ± 0.7
Plastic bow	56	8.9 ± 1.9	13	1.0 ± 0.3
Steel ring	85	4.7 ± 0.6	14	0.8 ± 0.2
Other devices	157	10.1 ± 1.3	34	2.3 ± 0.7
Total	1,248	11.0 ± 0.4	222	2.1 ± 0.2

* Cumulative rate per 100 cases during first year after insertion, with standard error.

MONTHLY RATES OF REMOVAL



CUMULATIVE RATES OF REMOVAL

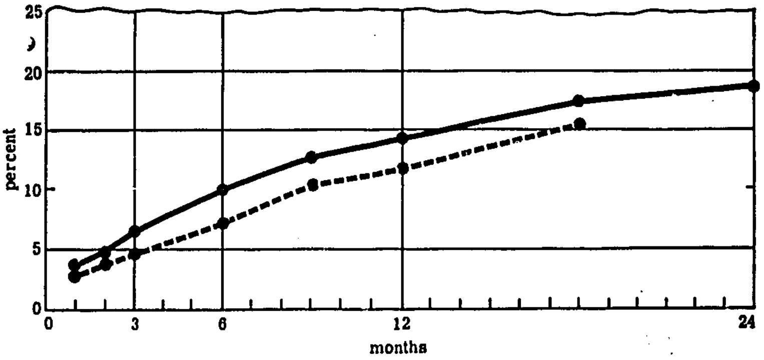


Fig. 3. Monthly and cumulative rates of removal on medical grounds.

The *medical reasons* for *removal* range from medical necessity, as perceived by the investigator, to complaints interpreted as related to the IUCD by the patient or her family physician. They also include preexisting and intercurrent conditions requiring treatment, but clearly unrelated to the use of the device. The most frequently reported reasons were bleeding (including spotting) and pain (including cramps, backache, and other kinds of discomfort). These two reasons, frequently reported together, accounted for 833, or about 2 out of 3 of the 1,248 patients experiencing a removal on medical grounds. Removals for medical reasons also include a small number of cases of discomfort to the male partner (41), attributed to the transcervical appendage of an IUCD, and all instances of pregnancy at insertion (36). They exclude removals after partial expulsion (classified as expulsion), and removals after an unintended pregnancy had occurred (classified as pregnancy).

Figure 3 shows monthly and cumulative rates of removal on medical grounds for the large spiral and the large loop. Compared with the expulsion rates shown in Figure 2 the monthly removal rates decline much less rapidly. Correspondingly, the cumulative removal rates at successive periods after insertion are represented by flatter curves. In other words, a larger proportion of removals for medical reasons than of expulsions occurs *after* the early months of wearing an IUCD.

The *personal reasons* for *removal* include all those considered relevant to the acceptability of intra-uterine contraception: fear of injury or cancer, lack of confidence, objections by husband or family physician (without a specific complaint), religious scruples, and a small group of removals at the patient's request without further explanation.

Devices were also removed because a pregnancy was desired, protection was no longer needed, or the patient departed from the locality of the study. Other removals were incidental to research procedures, such as endometrial biopsy, or the replacement of a device by another type or size considered more effective. Since none of these reasons is relevant to the acceptability of intra-uterine contraception, the removals assigned to them are not included in the computation of removal rates.

In 188 instances the IUCD was removed because the couple wanted a child. At the time of removal, the device had been worn for less than one year in 87 cases, between one and two years in 73 cases, and for a longer period in 28 cases. Excluding 79 instances in which the removal took place during the second quarter of 1964, or the investigator did not trace the patient, or the patient changed her mind, there remains for analysis a total of 109 *removals for planned conception*. The distribution of these removals by duration of follow-up and success in achieving pregnancy is shown in Table X. As indicated by the cumulative pregnancy rates in the last column, about 70 percent of the women conceived within six months and almost 90 percent within one year. Rates of this magnitude have been observed in samples of the general population. It would appear, then, that the wearing of an IUCD did not result in reduced fertility after it had been removed.

TABLE X

Removals for planned conception, by duration of follow-up and outcome

Duration in months	Number of removals by outcome		Total	Cumulative Pregnancy rate*
	Conceived	Did not conceive		
0–1	30	—	30	27.5
1–2	18	2	20	44.0
2–3	7	5	12	50.7
3–6	19	5	24	71.0
6–9	10	2	12	83.7
9–12	3	3	6	88.6
Longer	2	3	5	—
Total	89	20	109	—

* Pregnancies at end of period, per 100 removals.

Table XI presents data available for the first time on the association of expulsions and of removals for medical reasons with parity, i.e., with the number of children borne prior to the insertion of the IUCD. Pregnancies and removals for personal reasons were too few in number to permit this type of analysis.

Although the patterns are quite irregular and few of the rates differ significantly from the corresponding average for all parities, the incidence of expulsion as well as of removal for medical reasons tends to decline for most devices with increasing number of children. The expulsion rates for nulliparous women with the small spiral and the small loop are significantly higher than the rates for all women with the large spiral and loop, shown in Table VI. The corresponding differences in removal rates are not statistically significant.

TABLE XI

Rates of expulsions and removals for medical reasons, by type of device and parity

	PARITY				
Device	0	1	2	3	4 and over
			Expulsions		
Large spiral	21.9 ± 4.6	23.6 ± 2.4	16.0 ± 1.4	16.5 ± 1.6	16.4 ± 1.2
Small spiral	34.4 ± 5.0	34.0 ± 4.8	25.8 ± 3.4	35.2 ± 4.5	22.4 ± 3.6
Large loop	*	12.1 ± 1.8	10.5 ± 1.5	8.2 ± 1.2	6.9 ± 0.9
Small loop	25.2 ± 6.1	34.2 ± 4.5	18.8 ± 3.1	23.3 ± 3.5	13.2 ± 2.2
Plastic bow	*	7.5 ± 4.1	0.7 ± 0.5	1.6 ± 0.8	0.8 ± 0.4
Steel ring	5.0 ± 2.0	13.8 ± 2.2	9.7 ± 1.5	5.4 ± 1.3	8.9 ± 1.8
			Removals for medical reasons		
Large spiral	12.3 ± 4.2	16.5 ± 2.2	14.3 ± 1.4	13.7 ± 1.6	12.8 ± 1.3
Small spiral	12.0 ± 3.7	12.2 ± 3.4	11.9 ± 2.7	7.9 ± 3.2	12.1 ± 3.0
Large loop	*	14.6 ± 2.6	13.4 ± 1.8	11.0 ± 1.7	9.9 ± 1.1
Small loop	24.4 ± 6.3	15.0 ± 3.7	10.5 ± 2.6	18.1 ± 3.7	8.4 ± 1.9
Plastic bow	*	13.8 ± 4.8	7.6 ± 3.4	8.3 ± 4.1	4.4 ± 1.3
Steel ring	2.9 ± 1.7	3.9 ± 1.3	7.2 ± 1.4	4.5 ± 1.3	2.1 ± 0.9
			Number of cases		
Large spiral	150	546	1,014	763	1,550
Small spiral	124	138	202	137	182
Large loop	25	520	1,031	892	1,589
Small loop	77	146	195	194	314
Plastic bow	21	322	413	316	514
Steel ring	132	335	542	430	428

* Not computed. Number of cases too small.

Pelvic inflammatory disease (PID), subsequent to the insertion of an IUCD, was reported in 171 cases. The distribution of these cases by type of device is shown in Table XII, together with cumulative rates per 100 cases during the first year after insertion.

It is not known to what extent the differences in reported incidence of PID reflect variations in socioeconomic status and in sexual habits of patients, or in completeness of reporting, or diagnostic idiosyncrasies of investigators, or real differences between types and sizes of IUCD. It is believed that PID occurs more frequently among clinic patients than among private patients and that reporting is more likely to be complete in institutions which provide general gynecological care than in extramural contraceptive clinics.

Among the 171 cases reported as PID, only 63 were described as "severe" by the investigator, or the patient was ill enough to be hospitalized, or at least one of the following findings was reported: temperature of 38 °C or more or "fever" with or without chills, leukocytosis of 13,000 or more, a differential count of 80 percent or more polynuclear cells, or a sedimentation rate of 20 mm or more per hour. For many of the remaining 108 cases, including most patients seen in emergency rooms or by general practitioners, the available information is quite rudimentary. Twenty cases of PID, including 12 among the better documented and more severe group, occurred within one week after insertion.

In 71 cases of PID the device was removed, while in 85 cases the condition was treated successfully with the IUCD *in situ*. In the remaining 15 cases, the PID followed an expulsion of the device or a removal for other reasons. In more than half the cases diagnosed as PID, for which a complete report was submitted, a history of PID prior to insertion was obtained.

Patients lost to follow-up numbered 1,143, corresponding to 6.8 percent of all cases. This group is operationally defined as those women who were at least three months overdue for a scheduled examination and from whom no information was obtained by telephone, mail, or home visit. The cumulative rate of loss to follow-up per 100 cases during the first year after insertion is 8.4 for all devices combined and varies moderately between types of devices.

TABLE XII

Pelvic inflammatory disease, by type of device: numbers and rates

Type of device	Cases of PID	
	Number	Rate*
Large spiral	74	2.7 ± 0.4
Small spiral	14	1.6 ± 0.6
Large loop	34	1.2 ± 0.3
Small loop	11	1.5 ± 0.5
Plastic bow	8	0.6 ± 0.2
Steel ring	5	0.3 ± 0.1
Other devices	25	3.3 ± 1.0
Total	171	1.7 ± 0.1

* Cumulative rate per 100 cases during the first year after insertion, with standard error.

It is not known to what extent patients lost to follow-up are continuing and satisfied users or have discontinued use for one reason or another. In the computation of pregnancy rates, expulsion rates, and removal rates, their experience has been included from the month of insertion to the last month for which information was obtained, but not beyond. This procedure implies the assumption that pregnancies, expulsions, and removals occur with equal frequency, during a given period after insertion, among patients lost to follow-up as they do among those who remain under observation.

The over-all acceptability of intra-uterine contraception, from the objective-medical and the subjective-personal points of view, may be measured in terms of the cumulative rate of continuing use, i.e., the percentage of women wearing the device a specified time after first insertion, such as one year. Because the participating investigators differ markedly among themselves in their policies regarding reinsertion and because of changes from one type of IUCD to another, it is not feasible to compute comparable rates of continuing use from the numbers of closed cases actually reported. As an alternate procedure, a series of minimum rates has been estimated, based on the assumption that *no* routine visits and *no* reinsertions were made.

The highest minimum rate of continuing use, 83.2 per 100 cases, was computed for the steel ring, with an only slightly lower rate for the plastic bow. The corresponding rates for the large loop and the large spiral were 77.4 and 68.5, respectively, and even lower rates—in the vicinity of 60 per 100 cases—apply to the small loop and the small spiral.

If no contraceptive methods were used after expulsion or removal of an IUCD, most of the women who discontinue intra-uterine contraception would become pregnant within one year after insertion and would continue to conceive in subsequent years. Under this condition, the cumulative rate of continuing use may, therefore, be used as a rough measure of long-term effectiveness, as well as acceptability.

By promptly reinserting an IUCD at least once after an expulsion noticed by the wearer, the long-term usefulness of intra-uterine contraception can be increased by a few percentage points. The possible improvement is least for the plastic bow because it is associated with a low expulsion rate, and greatest for spirals, which have high expulsion rates; steel rings and loops are in an intermediate position.

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DISCUSSION

ACCEPTANCE

Introduction of intra-uterine devices

Dr. P. TALEGHANY (Assoc. Prof. of Gynecology, University of Teheran, Iran): I would like to say just a few words on how we started our program. Actually, we started inserting devices in our hospitals primarily for patients after childbirth and abortions. We had started contraception with the vaginal foam tablet, but we found they weren't satisfactory because they were causing many complaints about a great deal of heat in the vagina. Then we used oral pills. They were well accepted, but they are expensive. Then, through the courtesy of Dr Clarence Gamble, we saw the intra-uterine devices and started using them. We have found them extremely successful. We explained contraception to the patients in mass groups of about 40 or 50, and then let them choose the type of contraceptive they wanted. Usually, they started with the oral contraceptive and then switched over to the vaginal foam tablet but finally after a few months most of them wanted the intra-uterine device because they spoke to other patients who found it most satisfactory. We find this procedure more successful than forcing the patients to accept a certain type. They finally come round to the intra-uterine device. I would like to know how others get their patients to accept the type of IUCD that they use.

Dr. PAUL HARPER (The Johns Hopkins University School of Hygiene and Public Health, Baltimore): I'd like to ask the chairman if I might add a sort of footnote to what Col. Ziauddin has so excellently described about the work in a small area where we were. This work is being done by the group to which Colonel Ziauddin alluded, in a town of 12,500 people, about 25 miles from Lahore, in the center of an agricultural area. According to the census we took in 1962, the town contained 1,948 married women in the age group of 15 to 44 years; 832 of these women had three or more living children. These 832 women comprise the highly eligible group, but we have not yet been able to subtract from this group those women who are pregnant, or lactating, or have not been living with their husbands, or whom we believe are sterile, so we believe this group will be smaller later on.

Twenty-two months ago we began to offer contraceptive devices, and during this time there have been 105 insertions among the women who are residents of Lulliani. This is 5.4 percent of all the women in the child-bearing age group, and 12.6 percent of the highly eligible group of women. Incidentally, the literacy rate among the women who accepted IUCD is only 4 percent. In this village there has been a maximum effort and action in an educational program. It is of interest, however, that more than twice this number of insertions have been made in the health clinic for women who have come into Lulliani from the outside. Our educational program has been reaching them by word of mouth.

Dr. MAGGIE LIM (President, Singapore Family Planning Association): How do you manage to persuade people to accept this method in such large numbers?

Dr. P.Y. WEI (Dept. of Obs. and Gyn., National Taiwan University Hospital, Taipei): It's very easy. Our women know the government encourages it and the news is passed from friend to friend. We don't have too much of a problem with this.

Dr. S. **SUJAN-TEJUJA** (Reproductive Biology Unit, All-India Inst. of Medical Science, New Delhi): When we first introduced devices in our contraceptive study, we had a problem in getting patients. I think there is a lot to the attitude of the social worker, and then again acceptance is also promoted by word of mouth. Women who had heard of IUCD from their friends were offered the other contraceptives when they came to us, but they didn't want anything but the IUCD. People come to us from miles around for insertions and I think it's mostly due to word of mouth.

Relative acceptability of orals and IUCD

Chairman **TAYLOR**: We have a question as to the relative acceptability of orals and IUCD and the possibility of getting people to change.

Dr. C.H. **LEE** (Provincial Maternal and Child Health Institute, Taichung, Taiwan): I can report the data from the Taichung study. There we had what was called the "cafeteria choice" with a variety of contraceptive methods being made available—IUCD, the oral pills and traditional methods, such as foam tablets and condoms. In Taichung City and nearby the word spread regarding the loop, as Dr. Wei said. About 74 percent of those accepting contraception selected the IUCD, and only about 2 percent accepted the oral pills.

There was a cost factor involved here of course; for about 55 cents the patient could either have an IUCD inserted or buy enough pills to last only one month.

Attitudes of husbands

Dr. **TALEGHANY**: I would like to ask a question about the introduction of intra-uterine devices. Does the husband seek the device and then have his wife have it inserted, or do they just have it inserted without asking him? The reason I am asking this question is that in my country the wife cannot do anything without first seeking the permission of her husband. At first we had some difficulties in trying to explain the method to husbands, because they didn't have any idea where the device was going to be placed. Then we changed our technique. We would just talk to the wife and then have her bring the husband to see us. We told him that we were only placing a little guard to protect his wife from getting pregnant, but we didn't show the device. That was very successful.

Dr. A. **SATTERTHWAITE** (Dept of Obs. and Gyn., Ryder Memorial Hospital, Puerto Rico): We have some difficulties. Usually it's the woman who wants the protection and the husband who objects. We find that where the educational level is low, in the country areas, a man's potency and his manhood are judged by the number of children he has. Sometimes he will come and insist that the device be removed simply because he wants his wife to be pregnant again. Also many times when a man comes to the States for six months, he wants the device in the woman before he leaves. At first we did not ask the husband's permission but because of two instances where the husbands found out and were irate about it, we decided that we would have to ask for the husband's signature, or that of the marriage partner's, if it is not a legalized marriage. I have been inserting spirals with the warning that perhaps the husband will complain, because if I don't do this, they come running back saying, "My husband says take it out!" So I simply tell them beforehand, "Come back and we'll adjust it for you if your husband complains." This is one of the reasons I personally lean towards the loop, simply because they don't feel it, they're not aware of it, and so they don't worry about it.

Dr. **MARGARET C. N. JACKSON** (Medical Officer to Infertility & Contracep. Clinics, I.P.P.F., Crediton, England): I also had adverse reactions to the tailed devices by the husbands; quite a high proportion of the husbands noticed the tails but not the nylon threads.

Dr. Wei: In Taiwan we do not worry about the husbands. After insertion they know nothing. But in some cases the protruding tail was noticed, and some husbands objected to that, so we discarded the use of the spiral.

CLINICAL PROBLEMS

Contraindications

Dr. Herbert Hall (Dept. of Obs. & Gyn., New York Medical College, New York): In the cooperative statistical study, are there any computations on the use of IUCD by patients with previous benign endometritis or chronic cervicitis? How do you select patients?

Dr. Tietze (National Committee on Maternal Health, New York): This is entirely up to the investigators. All of them exclude acute inflammatory conditions and malignancies. Some make an effort to exclude other conditions, such as chronic inflammatory conditions, but some investigators do not apply such restrictions. It varies. I do not set the rules for the group. I just collect what they do.

Dr. C.M. Cassin (Grace-New Haven Community Hospital, New Haven): Are patients with a previous history of pelvic inflammatory diseases excluded?

Dr. Tietze: In each participating institution they are investigated, and to the best of my knowledge no one does so if there is no active disease.

Dr. Jackson: Just one comment from England, from a small rural area, on the selection of cases. They are self-selecting, because we are dealing with a highly fertile population and essentially they have no disease. Screening is done mainly by the practitioner who examines the women and very few have to be rejected—I can recall only one out of about 500.

Safety

Dr. Nicholson Eastman (Program Consultant, Physiology of Reproduction, The Ford Foundation, New York): I would like to ask Dr. Wei, with his vast experience, whether any accidents requiring hospital admission and intensive antibiotic treatment, or any leading to serious abdominal operations, have occurred. What serious accidents have you seen?

Dr. Wei: We had only one bad experience which was rather difficult to control. We had to remove the uterus, but this was only one case. The main danger is infection, which in our estimation is about 0.3 percent, but to me this is not high. There was one case of acute infection, but we controlled it very easily.

Dr. James M. George (Chairman, Medical Advisory Committee, Planned Parenthood Center, Pittsburgh): Have there been any cases of perforation of the uterus or the cervix with any of these devices?

Dr. **Tietze**: Yes, I know of six such cases among more than 16,000 insertions. They all seem to have happened at insertion. I don't know of any case where it looks as if the device perforated between insertion and removal by the physician.

Dr. **Gordon Perkin** (Assoc. Medical Director, Planned Parenthood Federation, New York City): Dr. Tietze, could you outline the incidence of other serious complications with these devices?

Dr. **Tietze**: We have tried to determine these but I do not believe my statistics are yet quite complete. Besides the six perforations that I mentioned, we have cases of pelvic inflammatory disease which I would classify as moderately serious. There were about 18 cases where the tail of the device was either embedded in the wall of the cervix or the vagina or had perforated the cervix. In these cases the investigator generally cuts the tail off, or removes the device and inserts a new one.

There were about a dozen cases of difficult removal, necessitating in most instances dilatation for removal. These cases involved the spiral less frequently than the loop because for a while we had trouble with the sutures on the loops. This has been remedied. There were also about a dozen cases where there was insufferable pain after insertion, so that the device had to be removed within the hour.

Dr. **Satterthwaite**: In general I feel that the insertion of the IUCD is not dangerous. For me, the greatest complications have been those associated with pregnancy. That's why I make the plea to the women to remove the device if they miss a period. Our women have not had many complications from early abortions.

Dr. **Tietze**: I would like to answer three questions put by Col. Raina. First, he was concerned with the frequency of the tail or the loop slipping up into the uterus as internal displacement; this occurred in approximately one percent of the cases that we have seen. Second, none of the investigators have reported any cases of erosion. Third, I want to point out that the pregnancy rate with the nylon ring is about three times the rate with the loop; the expulsion rate is about twice. On the other hand, the rate of medical removal is about half, so all these things have to be taken into consideration in comparing the nylon device with the loop.

Timing of insertions

Dr. **Peter Segal** (Planned Parenthood Association, Chicago): In reference to time of insertion, Dr. Zipper mentioned 50 days postpartum and 40 to 50 days after an abortion. How is insertion scheduled in relation to the menstrual cycle?

Dr. **Zipper** (Inst. of Physiology, University of Chile, Santiago): We insert a ring immediately after menses only to avoid insertion during pregnancy.

Dr. **George Andros** (Temple University Medical Center, Philadelphia): At Temple University we have attempted to determine whether intra-uterine devices can be inserted within a few days following delivery. The advantages of such timing are certainly obvious. During the last four months we have been doing a preliminary study and have inserted approximately 73 intra-uterine contraceptive devices during the first five days postpartum. We have a follow-up on approximately 60 percent of these patients. Approximately two-thirds of the devices used were Margulies spirals size 5, and the rest were Birnberg bows. Our results indicate that the rejection rate is probably in the same range as when they are inserted in the non-pregnant state or six weeks or longer postpartum. As for complications, we have had only one case of clinical endometritis. We have had another case of acute peritonitis that was probably pelvic in origin, but it occurred four months after insertion and was probably not related to the initial insertion.

Chairman TAYLOR: What day do you actually put them in? This is before they leave the hospital, as I understand it.

Dr. ANDROS: We try to put them in on the fourth or fifth day. Some of them have been placed as early as the third postpartum day. There were three expulsions in the hospital on the fourth postpartum day. These patients had the insertions on the third postpartum day, but they were reinserted before the patients left the hospital and were still in place at one month.

Chairman TAYLOR: Is there any other experience with insertions in the postpartum period?

Dr. MICHAEL S. BURNHILL (Brooklyn Jewish Hospital): We commenced a preliminary study of early postpartum insertion as indicated in the abstract, but we have now abandoned it and have advanced insertion to the moment of delivery. This study is based on hysterographic evidence of downward displacement of non-rejected devices at six weeks to three months postpartum, so we cannot assume because the device is present that it is affording any protection against pregnancy. Starting about last April, we began to insert the device immediately after delivery of the placenta. This has the great virtue of requiring no equipment, and so far not a single device has been rejected. Our experience has been rather small; hysterographic evidence in five or six patients has shown the device to be in place. We've also tried this in a number of cases where the patients have aborted; we have inserted the device immediately in three and they have retained it exactly as we placed it in the fundus.

Chairman TAYLOR: Is there any increased lochia when the device is inserted postpartum?

Dr. ANDROS: I and my colleague, Dr. Desai, have not noticed any increased bleeding.

Expulsions, removals, and reinsertion

Dr. TIETZE: I noticed that Dr. Zipper's material, in comparison with other studies, contains a very large number of partial expulsions, which he calls displacements, of which the wearer is unaware, and which are completed by removal and followed by reinsertion. I wonder if Dr. Zipper could tell us what criteria are necessary to diagnose a partial expulsion.

Dr. ZIPPER: We have included in our data of expulsions any protrusion of the device into the inner cervix or vagina. We feel that our clinic will have a higher expulsion rate than others, because we are experimenting, and many of our doctors have not had very much experience in fitting rings, and rings may be initially fitted not in the uterine cavity but in the cervix.

Dr. PETER ECKSTEIN (Dept. of Anatomy, The Medical School, Birmingham, England): What is the consistency of your device? Is there any reason to think that your ring becomes distorted once inserted into the uterine cavity?

Dr. ZIPPER: No, the nylon is very good. We have taken out our rings after they have remained four or five years in the uterine cavity and they have the original shape.

Dr. **Eckstein**: Can you X-ray it as it goes through the different phases, if there are any?

Dr. **Zipper**: We do not have the facilities to X-ray the patients. Besides, we don't think it's advisable to X-ray patients, because we can't be absolutely sure they are not in the first weeks of pregnancy.

Dr. **Jackson**: Dr. Satterthwaite, I believe I heard you say that you had eliminated self-examination among your patients. I would be very interested to learn why you did this, and whether you encourage any of your patients to examine themselves. We have eliminated it entirely in our clinics; I find it produces a lot of despondency and no reassurance.

Dr. **Satterthwaite**: The only women I've encouraged to make self-examinations are the few women who have previously used diaphragms and would be willing to examine themselves and were interested particularly in identifying the device. Most of the other women resist the idea of introducing a finger in the vagina, and therefore I just haven't talked about it.

Dr. **Tietze**: I have a question for Dr. Zipper. Among the 3,000 cases which he was good enough to send to us for analysis, I found a rather large number of removals and reinsertions of the ring. I would like to know whether this was done for purposes of investigation, to determine the condition of the ring, or whether Dr. Zipper feels that these rings should be taken out at intervals and if so, how long does he think they can remain in the uterine cavity.

Dr. **Zipper**: Removals were made for purposes of investigation. In general we feel that a ring need not be taken out unless medical reasons appear, because the chance that the women will become pregnant if you take out the ring is extremely high. I would say that removals because of medical reasons fall into two categories. The first, which we could call trivial reasons, includes removals of the device to treat cervicitis or any other chronic conditions. In these cases the device is removed and almost always followed up by reinsertion. The second category includes conditions which are considered serious by our investigators, such as pelvic inflammatory disease. Reinsertions are comparatively rare in this group.

Dr. **John Takeshita** (Population Studies Center, Univ. of Michigan, Ann Arbor): I want to emphasize that there is a social factor involved in the removal rate. Dr. Lee emphasized in his statement that there is need for more careful training of the doctors and the creation of a more intimate relationship between doctor and patient. This is quite justified on the basis of our experience. Our analysis showed that the removal rate declined as physicians gained confidence. For example, in the first month, February 1962, we had about 20 to 25 percent removals because patients asked doctors to have the IUCD removed for some discomfort or other complaints. With those who had insertions in June, the removal rate was reduced to about 12 percent. Our interpretation of this decline in requests for deliberate removal is that the public gains confidence in the device, and the doctors also presumably gain confidence and are less likely to recommend removal even if the patient may request it. We also have indications that the number of patients requesting reinsertion has increased with the progress of the program. All this supports our assumption that the social factor of gaining the confidence of the public and of the doctors themselves makes a good deal of difference in the acceptance of the device, and in continuation of use once it is inserted.

Dr. **Cassin**: We've had a resistance to reinsertion. I wonder if the same problem has arisen here in New York.

Dr. **Tietze**: Well, I cannot speak from personal experience because my study is based on what the investigators send me. I noticed however that the rate of reinsertion differs from investigator to investigator. There was one patient who had twelve expulsions with thirteen insertions and the investigator in question assures me that the woman demanded it. It's not his idea!

Dr. CARLOS MUÑOZ (Hospital A. Loayza, Lima, Peru): Is there reinsertion after pelvic inflammatory disease or after the expulsion of the IUCD?

Dr. TIETZE: Devices are not always removed for PID; patients are treated with the device in place. There are very many reinsertions after expulsion. In fact, I would say offhand that after first expulsions at least two-thirds are followed by reinsertion. Incidentally, the rate of re-expulsions after reinsertion is very high. The rate averages about 50 percent within the first twelve months, again computed on the life table method.

Finally, I would like to urge our colleagues in India and others too to adopt a standard method of recording their expulsion rates and removal rates. Unless this is done we'll never be able to compare the results achieved by the investigators in different countries.

Pregnancies; abortions

Dr. PAUL ENSIGN (Salt Lake City, Utah): I would like to know why we get a drop in the rate of unintended pregnancies after the first three months of use. With the Lippes loop, for instance, is there more chance of early pregnancy?

Dr. ZIPPER: With all the methods it's the same, and the rate of pregnancy drops after the first year. Maybe a group of very highly fertile women is selected out of any study by pregnancy in the first months.

Dr. ECKSTEIN: I got the impression from one of Dr. Tietze's tables that the conception rate is higher after the removal or withdrawal of oral contraceptives and lower after the removal of the traditional contraceptives. Have you any comparative figures?

Dr. TIETZE: That is probably true. There are a number of studies, involving over 200 pregnancies, and a number of informal observations, and the conception rate after the withdrawal of oral contraception is higher than you would find after the withdrawal of conventional methods. The figures we have observed for IUCD are approximately equal to those after the withdrawal of conventional contraceptives such as the diaphragm, condom, etc.

Dr. EDWARD E. WALLACH (U.S. Public Health Service, Tuba City, Arizona): Do you find in your statistics that the abortion rate following pregnancies with the device *in situ* differs at all from the figures on spontaneous abortions?

Dr. TIETZE: The percentage of abortions among IUCD *in situ* pregnancies was found to be approximately 50 percent. However, there is no doubt at all that many of these abortions were induced, but I can't tell how many.

Follow-up; discontinued cases

Dr. WALLACH: We deal mainly with the American Indian, specifically the Navajo, and our follow-up is rather difficult in some cases because of transportation problems. We offer several forms of contraception, including the oral form. If the patient doesn't return for a follow-up visit, we assume that she is no longer receiving medication and no longer falls within our figures.

However, when a patient with the IUCD doesn't return, how do we classify this patient, since she is potentially permanently infertile, in our calculation of pregnancies per hundred woman-years of exposure?

Dr. TIETZE: The question is a very interesting one from a statistical point of view, and I would say that your reasoning is perfectly correct. I can only tell you the way we have handled it. We classify a case as active until the date of the next scheduled visit, plus three months as a period of grace. If she doesn't come in then, we call the case closed as of the date of her last visit. This was adopted as a compromise. As time goes on, all the cases that don't come back are wiped out, and in the computation of the rates these cases are excluded. This implies that the pregnancy rates, the expulsion rates, and the removal rates are the same among the people who do not return as for the people who do return, but whether this is true or not, I cannot say. That is why I keep after my investigators to do a good follow-up.

Dr. Alan MARGOLIS (Dept. of Obs. & Gyn., University of California Medical Center, San Francisco): In view of the apparent popularity of the method in Jamaica and the small number of personnel on Dr. Williams's staff, and the apparent willingness of patients to report voluntarily when they have problems, I would like to ask Dr. Williams if he would be willing to dispense with follow-up.

Dr. WILLIAMS (Victoria Jubilee Hospital, Kingston, Jamaica): For the initial program we thought not. We did however propose to adopt a practice later in the program whereby patients would be inserted and then they wouldn't come back at all unless they had problems, but we propose to render a service program side by side with what we call the research program.

Chairman TAYLOR: This is a very important point. How often should the women be checked? My impression is that Dr. Shin was examining his patients very often in Korea. Certainly at this point paramedical help could be used, because if you have a tailed device your nurse or midwife could certainly do the routine checkups, if you want routine checkups.

Dr. G.T.M. CUMMINS (The General Hospital, Bridgetown, Barbados) : Several of the speakers are tending towards longer intervals between follow-ups. This may be justified, but I think one needs a note of caution. From our own experience with the insertion of Margulies devices we found that these lead to far more trouble in the immediate three months after insertion than any other device, and I think one has to follow up carefully in the next three months in order to avoid damaging the program. We have also had a lot of complaints on the part of the partner, or husband, and at this time the patient needs a little reassurance. I think if this is all the follow-up does, it is a lot.

Dr. P.B. SEGAL: I'd like to ask Dr. Williams if he has had a chance yet to analyze his series from the important point of view of the effect of opening his clinic on the rate of return of patients for postpartum visits.

Dr. WILLIAMS: No, except to say that in general, perhaps 90 percent of these patients would not have had postpartum examinations. It is clearly impossible for us to take fourteen thousand patients in a year. We can only look at patients of a very highly selected sort. I think an important development that has come out of our clinic has been that we have made available postnatal examinations to women who would not normally receive a postnatal examination.

Types of IUCD

Dr. M.L. STONE (Dept. of Obs. & Gyn., New York Medical College, New York): For completeness I would like to add to Dr. Robert Hall's excellent comparative study of three intra-uterine plastic devices a fourth device which has received very little attention at this meeting—the Hall stainless steel ring. I've had experience now for over a year and a half in a voluntary hospital clinic in New York City in the use of the stainless steel ring. Dr. Tietze's statistics show how favorably this device compares with all the others. It has the lowest incidence of infection reported by anyone. It has also low incidence of removal for medical reasons. The pregnancy rate is roughly equivalent to that shown by Dr. R. Hall for the other groups.

It has certain other decided advantages which I think should be noted. First, the cost is quite favorable. The cost is at present roughly two dollars. The ease of detection of this wholly intra-uterine device can't be emphasized too greatly. Since it is made of metal it can be detected more easily than plastic devices, by means of a uterine sound gently inserted into the uterus. With a little experience, X ray is very rarely necessary.

Our studies on endometrium have shown the steel ring to be a very safe and very effective device. I should like to make a plea to those of you who are contemplating beginning clinics that you use stainless steel as well as plastic.

DISCUSSANT (not identified): I have enjoyed hearing Dr. Hall's presentation. However, there are a few questions I would like to ask him.

First, who inserted the devices—one individual or a group of individuals? Was there any randomizing in these insertions? This is important because in our experience a man using one device over a period of weeks increases his confidence and reduces his chances of failure. In order to have a valid comparison of the different devices, I believe an alternation of the types of device among the individuals doing the insertions is necessary.

Secondly, my experience is limited, since I have been using the Margulies spiral primarily, and have inserted about 300 of them. There is one known pregnancy and a drop-out rate of about two percent. I would therefore say that the Margulies spiral should not be dropped until we have more evidence.

Another point that I think is important is that the women in Dr. Hall's series were primarily postpartum. This is only one of the big groups we have to deal with today. There are individuals who had their last pregnancy as long as five or even eight years ago. There is also a large group of nulliparas who are in an entirely different category, which Dr. Hall did not mention at all.

Dr. Robert HALL (Dept. of Obs. & Gyn., Columbia-Presbyterian Medical Center, New York City): As for who did the insertions, initially I did them all. This reminds me of one of the points Dr. Williams made in his report on Jamaica, about the manpower needed to run a clinic like this. I started seeing about 20 patients a day. That was a year and a half ago. Now we are seeing about 75 a day and it takes two of us and two secretaries to run it, because we not only are seeing new patients but we are seeing patients with problems and we are seeing the annual checkups, and this is just going to snowball every year. So I've had help from Dr. Susan Williamson who has had varied experience and who is now very experienced in inserting hundreds and hundreds of devices. The two of us have done all of the insertions. As for the confidence that you mentioned, I think the confidence is high.

As to whether or not we randomized our choice of various types of devices, I refer again to Figure 2 in my paper. Use of the various types was to some extent dictated by circumstance. We initially intended to alternate spirals and loops but we had difficulty at first in getting loop equipment and could not put in as many as we intended. As the figure shows, seventeen months ago we were putting in mostly spirals but also some loops of size 1 and 2. We started using bows in September 1963, and have now accumulated a year of experience with them. We tried to randomize, but it's difficult.

As for the Margulies spiral, I didn't say necessarily that it should be abandoned. I said that from my experience at Sloane Hospital with about 2,000 cases in a comparison of the relative merits of three devices, the spiral certainly appears to be the worst in most respects.

As for parity, almost all of our patients were parous. I share Dr. Tietze's opinion rather strongly that this is not a type of contraception suited to the nullipara.

Dr. Deborah BAUMGOLD (Margaret Sanger Research Bureau, New York City): I would like to give you our experience with the Margulies, Birnberg, and Lippes devices. We don't use them alternately. We started using the Margulies spiral on 50 patients, then we used 250 Birnberg bows, and now we have used 250 of the Lippes loop. Our findings on effectiveness and side effects match well with Dr. Hall's.

PERSONNEL AND ADMINISTRATION

Use of general practitioners and paramedical personnel

Dr. JACKSON: In the large-scale program in Taiwan, were all the insertions done by doctors, essentially gynecologists, or were other personnel used?

Dr. WEI: In the selected townships we would have a doctor and he would have other personnel under his supervision. The reason we chose the particular townships was because there were enough doctors in them who could supervise others.

Dr. Ralph RICHART (Dept. of Obs. & Gyn., College of Physicians and Surgeons of Columbia University, New York City): Dr. Zipper, what proportion of your devices are inserted by medical personnel and what proportion by paramedical personnel, such as midwives?

Dr. ZIPPER: I think that most of them are inserted by medical personnel. We have two midwives—one of them especially is extremely clever and expert in inserting devices.

Dr. Hugh J. DAVIS (Dept. of Obs. & Gyn., The Johns Hopkins University School of Medicine, Baltimore): Dr. Tietze, as we move into the increasing use of contraceptives for large-scale population control, it becomes increasingly important to know how serious the bottleneck of too few medical specialists is. I would like to ask you therefore whether you have at this time even an impression that the failure rates or complication rates rise as one goes from the specialists to the general practitioners and into the area of application by paramedical personnel.

Dr. TIETZE: All our investigators are well-trained physicians, so I'm not qualified to answer that question.

Dr. Shin mentioned a number of contraindications which are considered important in his program. Obviously, the question of contraindication is closely related to the problem of whether paramedical personnel, midwives, etc., could be used in such a program. I would appreciate his views on this subject.

Dr. SHIN (Dept. of Obs. and Gyn., Seoul National University College of Medicine, Korea): In Korea a program of using other medical personnel is now under consideration. After a doctor examines and finds no contraindications other paramedical personnel might be able to do the insertion.

Dr. TIETZE: But the examination takes much longer than the insertion. If you have a doctor there to screen the patient, then you might as well have him do it.

Dr. SHIN: Well, in my country the program works this way: a doctor goes out and screens the patients, and then the insertion is left to midwives.

Dr. ARUMUGAM THARMARATNAM (State Gynecologist and Obstetrician, General Hospital, Malacca, Malaysia): It is obvious from the reports so far that the use of the current intrauterine devices is associated with a number of complications. All these complications will ultimately have to be dealt with by gynecologists. As the use of these devices becomes more widespread throughout the developing countries the gynecological complications will increase. I wish to ask Dr. Shin if, with the gynecologists now available in Korea, they will be able to deal with all of the complications which might occur?

Dr. SHIN: We feel that we can use the device safely.

Chairman TAYLOR: Excuse me, Dr. Shin, but the chair would like to beg your indulgence. I think that those who are enthusiastic about the use of IUCD believe that the complications from them will be much fewer than the present problems of treating induced abortion or of repeated pregnancies and it might therefore be argued that the work of the gynecologist will be definitely reduced. At least this is a possibility.

Dr. STEPHEN POLGAR (Director of Research, Planned Parenthood/World Population, New York City): I'd like to come back to the question of semi-professional workers and ask the people who have commented on this earlier today whether paramedical personnel can be used for follow-up?

Chairman TAYLOR : This is a very important question. Would anyone care to reply to it? The question is whether midwives can do part of this work, as compared with physicians who are specialists.

Dr. RALPH TEN HAVE (Maternal and Child Health Division, University of Michigan School of Public Health, Ann Arbor ,Michigan): I don't think there is enough information yet to give an answer. I think there is need for careful studies, very slowly developed with lots of supervision at first, to see how things develop. If they are well reported and can be duplicated in various countries, then that question can be answered.

Dr. TIETZE: I would like to say a word about training the general practitioner. I don't think it will be possible for governmental programs or other organized programs to expand and reach the mass of the population unless the majority of physicians are convinced that this is a good method, because people listen to their doctors and the opinions of doctors sift down into the community to the poor people who, themselves, may not be able to go and see a physician.

Therefore, the general practitioners or doctors must be familiarized with the method, and frankly, I think they will be far more willing to familiarize themselves if they have an opportunity to make an honest evaluation. I think it's very important that there should be a program directed straight to doctors, and these devices should be made available through them so that they become a part of their general practice.

Training of personnel

Dr. R.M. CUSHING (Women's Hospital, New York City): I'd like to ask Dr. Shin to tell us a bit more about the training program for general practitioners, and then I'll tell you about some of our thinking at the moment and get your reaction to it.

How long does a doctor attend a training program? Do you train him individually or in groups, and if in a group, how large a group? What do you consider to be the minimum number of insertions before a doctor is considered qualified? We have a number of thoughts on this. One is that you can teach a man the mechanics of insertion by having patients, but you cannot demonstrate follow-up with the few patients who happen to appear during the short time that he's attending the course, so that you may have to resort to a set of case records of women coming back at different stages and seeing what he can learn from that and how to handle them.

The other point is that the program of training doctors should not be limited to the IUCD itself, but should be more comprehensive and include other types of family planning. It does not seem appropriate to have a service that's exclusively IUCD, as some of the women may have medical complications which contraindicate pregnancy. If devices do not work for them there should not be a gap in contraceptive service.

Dr. SHIN: Our training of the doctors takes two days—one day of lectures about family planning and the general techniques of contraception, and one day handling the device. Follow-up is stressed more in the training of field workers.

Chairman TAYLOR: That's an interesting point. Dr. Shin, you think two days is sufficient to train the general practitioner? I am not objecting to this, but I'm interested in your opinion.

Dr. SHIN: Well, we select physicians who have some experience.

Chairman TAYLOR: But, it's your view that it only takes two days to train him?

Dr. SHIN: Yes.

Dr. CUSHING: I just want to ask again if you have the man trained individually, or in a group, or how do you do this? The whole question of setting up a national training program and training centers requires that the centers have enough patients coming on any given day for you to have material.

Dr. SHIN: Yes, we do training in groups, and some individually. We set up five training centers in South Korea and those doctors who live near the training center come for one day of lectures and one day of practice in putting in the loops.

Dr. M. KARIM (Dept. of Obs. and Gyn., Einsham University, Cairo): At what level do you start training the nurses who are essential to your program? Are student nurses given instruction as part of their general training?

Dr. SHIN: The government asked each of us to give special lectures on family planning to the midwives' associations and the nurses' organizations, which are regularly holding meetings for family planning and training.

Dr. KARIM: Is it basic now for countries that sponsor family planning to actually put the training in their medical and nursing curricula?

Dr. SHIN: I do not know about other countries, but for us I think it is essential.

Dr. CUMMINS: I am referring to Dr. Shin's statement that two days are sufficient to train a physician. I think programs will have to be developed where trainees go out and deal with large numbers of patients and reassure those who have minor complaints, and deal with major complications. There is a big difference between specialists and general practitioners, and I think it would take more than two days for the average general practitioner to acquire the skill. I think this is very important, because in the end paramedical personnel, adequately supervised, will have to be used to get the mass attack which will be necessary to put effective programs in operation

Mobile teams and mobile clinics

Dr. Franz ROSA (National Institute for Child Health and Human Development, Bethesda, Maryland): I was very impressed with the work of Dr. Saigal, especially since I'm sure that it must have been done under very difficult circumstances, at least according to my experience in Ethiopia and Pakistan.

I think very careful consideration is needed on what mobile clinics should be used for and what they should not be used for. Most mobile units run into a great deal of expense: the roads are poor; the distances are great, involving a great deal of time spent in travelling; you have very difficult living conditions, and inadequate facilities for your staff. You have to worry about your supply of electricity, heat, and water, and you have also a great deal of difficulty with mechanical maintenance.

I do think a small mobile unit is fine for survey purposes, for certain investigations, and for supervision of permanent facilities in an area, but mobile clinics won't support a permanent service program in an area.

Dr. S. WISHIK: I think a distinction should be made between the terms "mobile clinic" and "mobile team." It's a very big distinction because the first carries the equipment along, and the other really means only that you are transporting personnel.

You might think of the situation as falling into three separate circles. Within the innermost circle are the dense urban areas which are easily accessible and present no difficulty. Then there are intermediate areas, which are somewhat less accessible but can be reached by the methods presented by Dr. Ten Have and Dr. Saigal. Then we should recognize peripheral areas that we cannot hope to reach with the IUCD, but there are other methods that might be more applicable for those areas.

Governmental auspices: Chile and Korea

Mrs. L.W. BULLITT (Population Consultant, U.S. Agency for International Development, Washington, D.C.): It says in the abstracts that the health authorities provided for the first time the necessary medical resources to insert 30,000 rings in the area of Santiago. Are these health authorities part of the government? Are these 30,000 rings being put in with government facilities, or what is the situation?

Dr. ZIPPER: That's very interesting. In our country we have a national health service and private medicine. The facilities to insert rings mean in fact a provision to pay physicians and paramedical personnel. The Divisional Director of Health in Santiago has paid ten physicians to go around to every clinic in the city to do a demonstration, and has also provided funds for ten to twenty midwives and paramedical personnel. The 30,000 rings were paid for by the government.

Dr. MARSHALL C. BALFOUR (The Population Council): I would like to answer a question, rather than ask one.

When Dr. Berelson presented his statement and figures on the programs of various countries, the gentleman sitting next to me asked me why Korea has succeeded so well in a matter of a few years. Because of his modesty Dr. Shin might not wish to answer the question, and I will try to do so.

In the first place, the government of South Korea, which came into power in May, 1961, was a military government. This government was so acutely aware of the danger of their population problem that they and the young cabinet members in the government were determined to do something about checking population growth. Therefore, they made a firm policy decision in favor of population study and control, and they appropriated money for this purpose. Each year since then the government's appropriation has doubled and at the present time the appropriation for family planning is equivalent to about $1,500,000.

The second reason is that South Korea has a reasonable number of outstanding medical and public health personnel in its Ministry of Health and medical schools and in its Planned Parenthood Federation. They have given the leadership to put the program across.

Further, Korea is in a better position than many other Asian countries in that they have a fairly adequate number of medical personnel to implement the program. They have some 10,000 graduate doctors, some 8,000 midwives, and six or seven thousand nurses. As Dr. Shin has told you, they have health centers pretty widely distributed throughout the country and at the moment there are 1,700 full-time trained family planning workers of different qualifications throughout the country. Every township of 10,000 has one full-time worker.

I would say that South Korea has its problems as other countries have. There is some bureaucracy, but they don't have as much bureaucracy as some other countries, including the United States. However, I believe that the favorable factors I have mentioned account for why Korea has been able to succeed so well.

PART II

BIO-MEDICAL STUDIES : SIDE EFFECTS AND MECHANISM OF ACTION

SUPERIMPOSITION HYSTEROGRAPHY AS A TOOL IN THE INVESTIGATION OF INTRA-UTERINE CONTRACEPTIVE DEVICES: PRELIMINARY REPORT

by

MICHAEL S. BURNHILL, M.D. and CHARLES H. BIRNBERG, M.D.*

Fifty-five years have passed since Richter[6] introduced a coil of silk as an intra-uterine contraceptive device. Today little is known about their mechanism of action, the causation of side effects, or the reasons for ejection. Differences in the pregnancy rates, side effects, and ejections have been noted by different observers using the same device.[2,4,9]

The present study was undertaken in February 1964 to determine if the position of an intra-uterine contraceptive device (the "bow") in the endometrial cavity has any possible relationship to pregnancy, ejections, and side effects.

Materials and methods

Seventy private patients were fitted with intra-uterine contraceptive bows of varying size (Figure 1). Prior to the present study the patients had been examined at six-month intervals and an X-ray film of the lower abdomen was made to determine the presence of the device within the patient. All examinations now include a two-film hysterogram. These are taken two months after the insertion of the device and one year later. Patients who had a device inserted prior to the present study have a hysterogram performed at their next regularly scheduled follow-up examination.

The hysterographic technique employed has been described.[1] The first film is taken after 1/2 to 3/4 milliliter of iodized oil (*Ethiodol* Fougera*) has been introduced; this picture shows the device clearly with some of the surrounding cavity of the uterus. Four milliliters of contrast medium are then added; the second film usually outlines the entire uterine cavity and obscures the intra-uterine device. Careful superimposition of the two films enables one to see the exact relationship of the device to the surrounding uterine walls. For clarity in publication the devices have been stippled in ink on the X-ray plates.

Results

Seventy-five hysterograms were made. Four patients had two different hysterograms performed. Four of the hysterograms were technically poor and could not be read.

Each hysterogram was analyzed for the following factors: (1) tubal visualization—unilateral, bilateral, or none; (2) percentage of fundus covered by the bow, classified in four groups: 0-25, 25-50, 50-75, and 75-100 percent covered; (3) presence of wedge-shaped defects in either lower or upper uterine walls ("prong signs"); (4) orientation of the bow—inversions, horizontal placements, or distortions of shape; and (5) characteristics of the uterine cavity—length, width, congenital abnormalities, or submucous fibroids.

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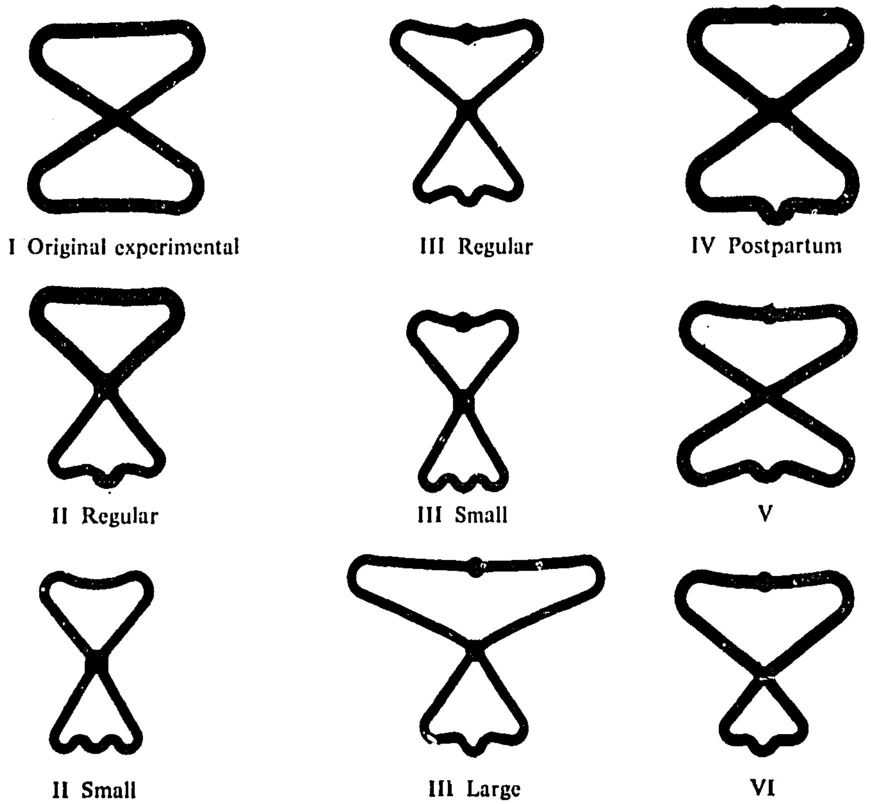

I Original experimental
III Regular
IV Postpartum
II Regular
III Small
V
II Small
III Large
VI

Fig. 1. Evolution of the intra-uterine bow. Bows (actual size) used in hysterography study.

1. Tubal visualization. No special effort was made to visualize the Fallopian tubes. Indeed, the X-ray picture was taken as soon as the contrast medium was injected. Despite this, 35 of the hysterograms showed bilateral tubal visualization and in 16 others unilateral visualization was noted. Of the remaining hysterograms 13 showed bilateral cornual spasm, 4 showed cornual occlusion, and 3 films showed the presence of an incomplete abortion so that no statement could be made regarding the Fallopian tubes. It seems to the authors that 15.5 percent of hysterograms demonstrating cornual spasm is an unusually high percentage in a group of fertile women. This may be but an indication of hypermotility being present as part of the contraceptive effect of the intra-uterine devices.

2. Percentage of cavity occupied by device. Table I shows percentage of the cavity occupied by the device according to the size of device used. It also gives the average number of weeks that the device had been *in situ* before the hysterogram was taken.

In 35 (50 percent) of the patients X-rayed, the device occupied more than 75 percent of the fundus; 18 (26 percent) of the patients had a device that occupied between 50 and 75 percent of the fundus; 10 (14 percent) had a device that occupied 25 to 50 percent of the fundus; in the remaining 7 (10 percent) less than 25 percent of the fundus was occupied. Two of these patients were in the process of aborting. Two had devices inserted in the early puerperium. Three were discovered to have the device within the cervico-isthmic canal. Two of these last three hysterograms were taken because the patient complained of menorrhagia. Figures 2 through 8 show examples of varying types of fundal coverage.

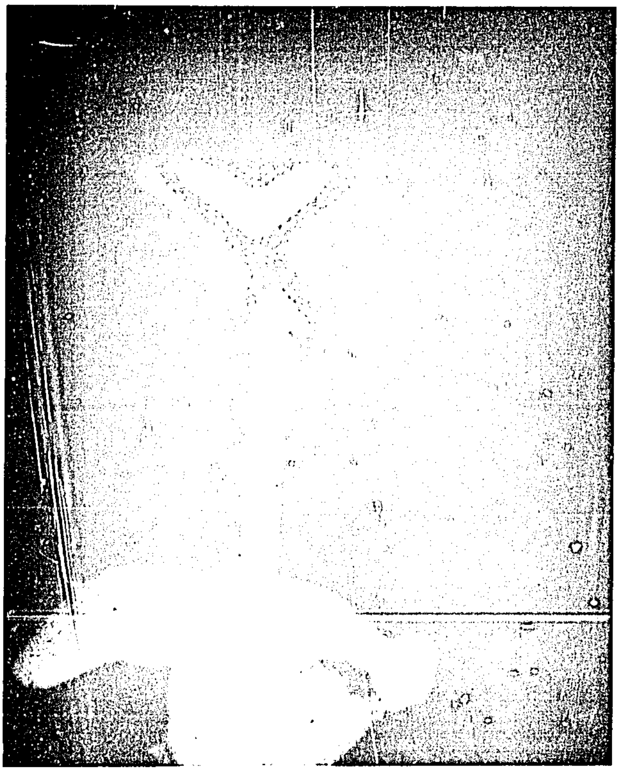

Fig. 2. Type III bow *in situ* 51 weeks, showing 100 percent fundal occupancy, and moderate "prong sign" at cervico-isthmic junction.

TABLE 1

Percentage of fundus occupied, by size and type of bow used

Bow Type:	I & IV	II Regular	III Regular	II & III Small	V	VI	Total
0–25%	3 (16)*	—	3 (39)	1 (26)	—	—	7
25–50%	1 (12)	1 (73)	3 (33)	2 (52)	1 (12)	2 (18)	10
50–75%	1 (32)	5 (73)	8 (32)	—	4 (13)	—	18
75–100%	5 (36)	5 (62)	12 (37)	1 (29)	8 (11)	4 (13)	35

* Figures in parentheses give the average period (in weeks) that the devices have been *In situ.*

3. *Prong signs.* Twenty-one (30 percent) showed defects in the lower uterine segments of the type seen in Figures 2 and 3. The larger defects were usually associated with mild menorrhagia or cramping. Seven (10 percent) showed similar defects in the mid or upper fundal walls.

4. *Orientation of the bow.* Six of the bows were found to be lying horizontally within the uterine cavity. Figure 4 shows an example of this placement. The bows are retained well

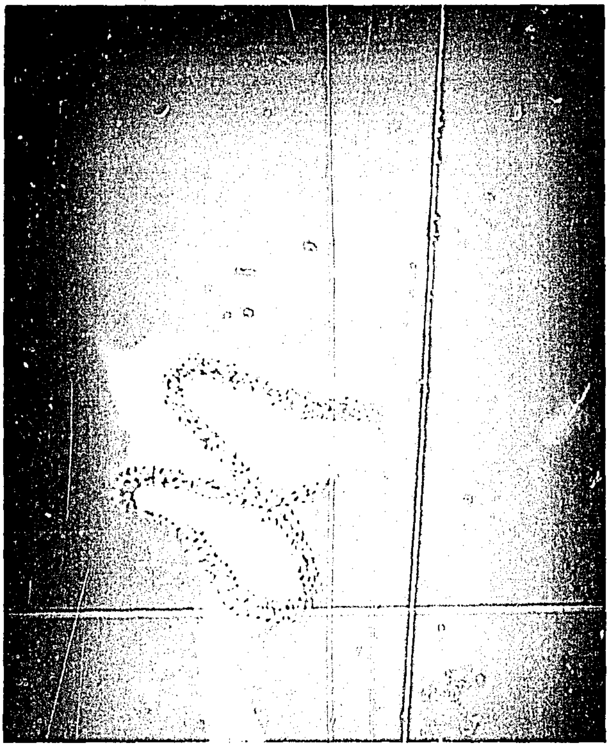

Fig. 3. Type V bow *in situ* 7 weeks. This bow was inserted manually after incomplete abortion. Note "prong signs" in mid and lower segments.

in this position, without side effects. Three of the bows were found to be inverted. One bow was seen to have its lower triangle still folded in the lower uterine segment.

5. Types of uterine cavity encountered. Thirty-seven (53 percent) of the cavities showed a normal triangular configuration; 17 (24 percent) showed a large triangular cavity. Four uteri had broadened cavities with bicornuate tendencies. Four had narrow conical uterine cavities. Two hypoplastic cavities were detected. The remainder showed defects due to fibroids or pregnancies, or could not be classified. Figures 2 through 8 show examples of the cavities encountered.

Discussion

Verhagen[10] and Rozin[7], in using hysterography, observed non-radiopaque contraceptive devices within the endometrial cavity, but they were not particularly interested in the functioning of the devices as contraceptives. Carleton and Phelps[3] in 1932 showed that intrauterine contraceptive devices in rabbits protected the area lying immediately adjacent to the device, but areas either above or below the device were not protected. The present study has shown that in some patients an abnormally shaped or enlarged uterine cavity, or a silent downward migration of the device, may leave large areas of the endometrial cavity unprotected by the contraceptive device.

Haire[4] in 1930 observed that some gynecologists had a very high incidence of side effects

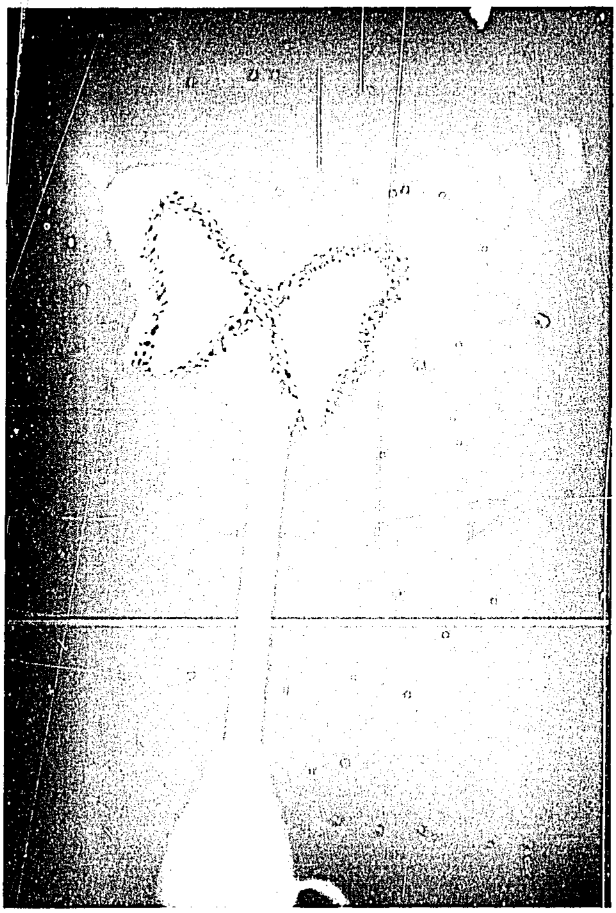

Fig. 4. Type V bow *in situ* 11 weeks, showing 100 percent occupancy. The bow is in a horizontal position in an arcuate fundus.

with the Gräfenberg ring, though he had little difficulty with them himself. Correlation of the clinical history with the radiographic finding of the "prong sign" showed that most patients demonstrating this sign had demonstrated marked increase in the usual side effects of mild menorrhagia, metrorrhagia, and cramping. The side effects may be due to pressure of the device against the sensitive cervico-isthmic junction.

Malkani,[5] and Siegler and Hellman[8] have shown tubal patency in small numbers of patients who have been fitted with an intra-uterine spiral. Seventy-two percent of the cases here reported showed unilateral or bilateral tubal patency, confirming their findings.

The present study shows that the mere presence of an intra-uterine contraceptive device within the endometrial cavity gives no assurance of adequate fundal coverage to afford a good contraceptive effect. Improper initial placement, silent partial ejection, abnormally shaped or enlarged uterine cavities all lower the contraceptive effect of the device.

Summary

A simple two-film hysterogram was performed 75 times on 70 private patients. Partial or

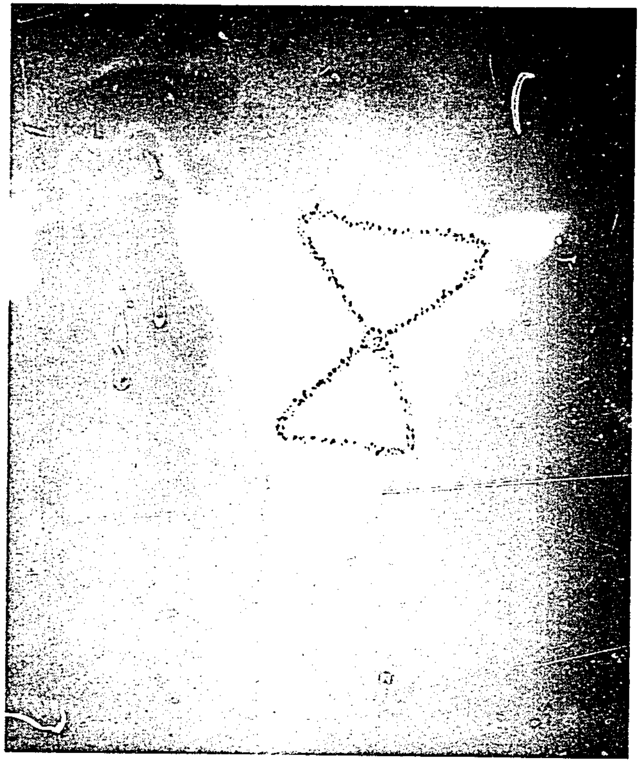

Fig. 5. Type III bow *in situ* 30 weeks. The bow occupies 50 percent of an abnormally large fundus of normal shape.

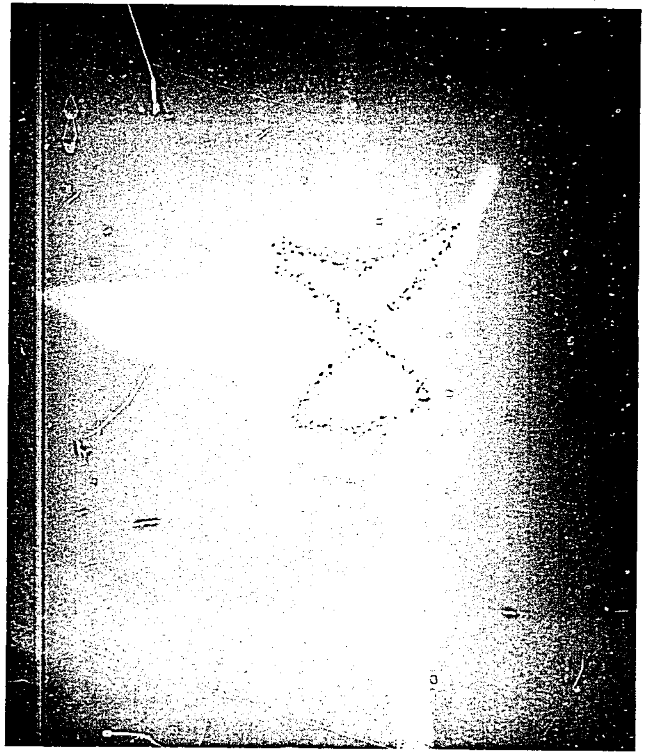

Fig. 6. Type III bow *in situ* 28 weeks. The bow occupies 50 percent of an extremly broadened fundus.

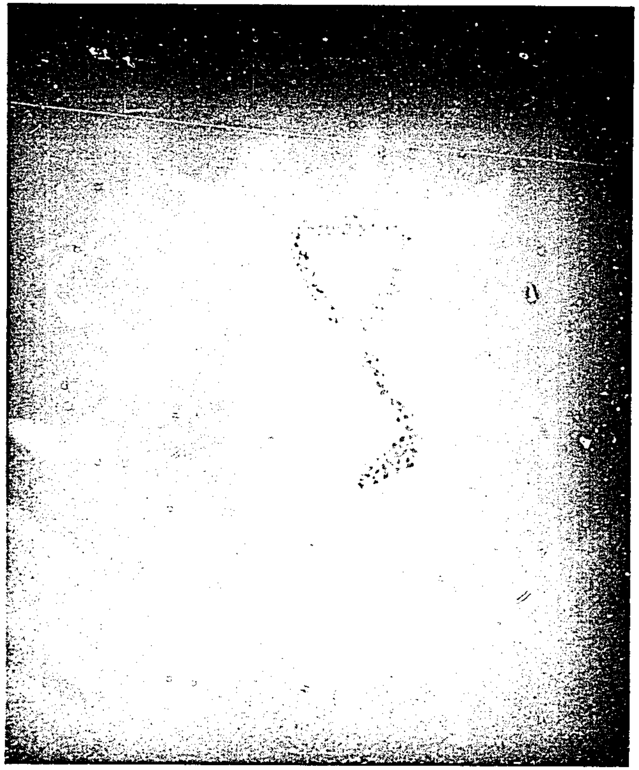

Fig. 7. Type III small bow *in situ* 29 weeks. The bow occupies 50 percent of a small T-shaped cavity, with the lower triangle folded.

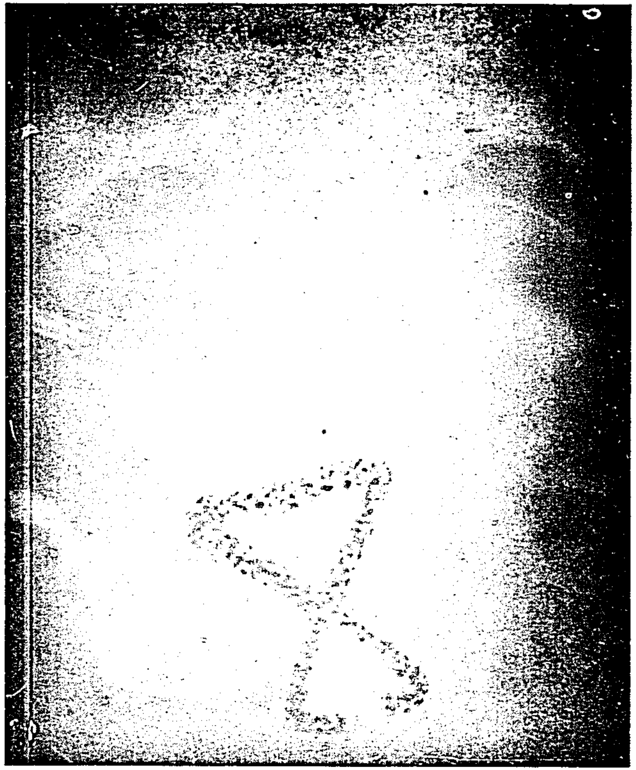

Fig. 8. Type II bow *in situ* 73 weeks. The bow occupies the lower uterine segment, with the lower triangle apparently in the upper cervical canal.

complete tubal patency was found in 72 percent of the hysterograms. In 51.5 percent of the hysterograms more than 75 percent of the fundus was protected by the contraceptive device. In 26 percent between 50 and 75 percent of the fundus was protected.

Thirty percent of the patients showed wedge-shaped defects in the cervico-isthmic portion of the hysterogram. This "prong sign" was usually associated with an increase in side effects.

Hysterography is suggested as a tool for studying the effects of intra-uterine contraceptive devices, and as a means of fitting devices in those women in whom a better contraceptive effect is desired.

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UTERINE CAVITY MEASUREMENTS IN RELATION TO DESIGN OF INTRA-UTERINE CONTRACEPTIVE DEVICES*

by

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The dimensions of the human uterine cavity have been measured in scattered morphological exercises for more than a century,[1] but the bulk of this information is not pertinent to the design of intra-uterine contraceptive devices. Prior studies were derived largely from pathological specimens, autopsy specimens, or fixed specimens, utilizing molding techniques of doubtful validity. Data on the characteristics of the normal premenopausal parous uterus are scant, although this group is the prime target for contraceptive management.

Early published studies which cast light on the dimensional characteristics of the human endometrial cavity include those of Guyon[2] and Hagemann.[3] Some examples of Guyon's investigation, published in 1858, are shown in Figure 1; they were produced by injecting the uterine cavity with a resinous material. Hagemann made similar casts by injecting molten type metal into postmortem specimens. The study of Mauclaire[4], published in 1897, is representative of the inapplicability of these historic investigations in seeking to establish the dimensional characteristics of the parous human uterus. Mauclaire studied a total of 85 fixed autopsy specimens, but only six specimens were obtained from normal premenopausal multiparae, not to mention the alterations produced by the process of fixation *per se*. There is a hiatus in further studies until 1929, when Nishizaki[5] prepared some uterine casts incidental to the design of instruments for cornual electrocautery. Unfortunately, his molds were prepared by tamping dry plaster of paris into the endometrial cavity, resulting in molds of poor quality.

With the resurgence of interest in intra-uterine contraceptive devices, the actual dimensions of the uterine cavity would seem to be important in designing and fitting intra-cavitary contraceptives. Yet, although some of the design characteristics of intra-uterine contraceptive devices (INCON's) currently in use suggest attempts to conform to the contours of the uterine cavity, there have been no systematic studies published presenting such data. Indeed, the morphology of most devices suggests emphasis on ease of insertion of a standard empiric design. The fact that such empiric designs function reasonably well as low-cost, low-motivation contraceptives must raise the question whether consideration of variants in normal uterine configuration might lead to refinements in design and perhaps to improved effectiveness.

Materials and methods

Twenty-five fresh uterine specimens, removed by vaginal hysterectomy four to six months postpartum, were utilized in this investigation. All specimens were grossly and histologically

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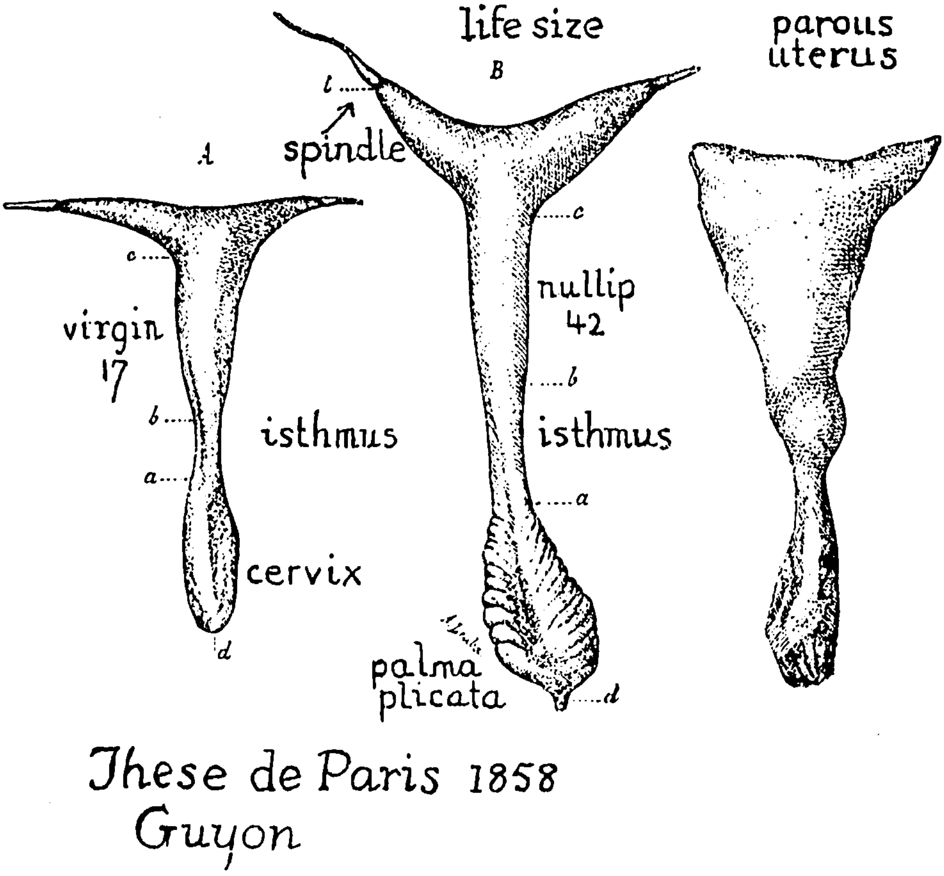

Fig. 1. Historical uterine casts prepared by Guyon (1858) demonstrating various types of uterine cavity morphology by resin injection technique.

normal. Molds of the uterine cavity were prepared by suspending the specimens, fundus down, and instilling 8 cubic centimeters of silicone rubber compound. This volume produced moderate distension of the uterine cavity, which was manifested by slight bulging of the anterior and posterior fundal walls. Digital compression of the fundus caused immediate backflow around the instilling cannula. The cannula was removed and excess material encouraged to reflux freely through the cervical canal. The silicone compound was solid enough within one hour to allow removal; in twenty-four hours the mold was of a solid rubbery consistency permitting easy manipulation (Figure 2). The uteri were opened in the sagittal plane, the molds delivered, and permanent impressions made in plaster of paris for analysis.

In order to provide a meaningful expression of the dimensional characteristics of such a variable object as the human uterine cavity, a standard system of measurements was devised. Arbitrarily, the transverse dimension of the uterine cavity at a distance one centimeter proximal to the top of the fundus was determined, the *transfundal superior* measurement. Similarly, a second transfundal measurement was made at a point two centimeters proximal to the top of the fundus, and this was termed the *transfundal inferior* measurement. In all cases the transfundal inferior measurement was above the level of the internal os, as determined by the narrowing of the passage and the appearance of palmae plicatae. The validity

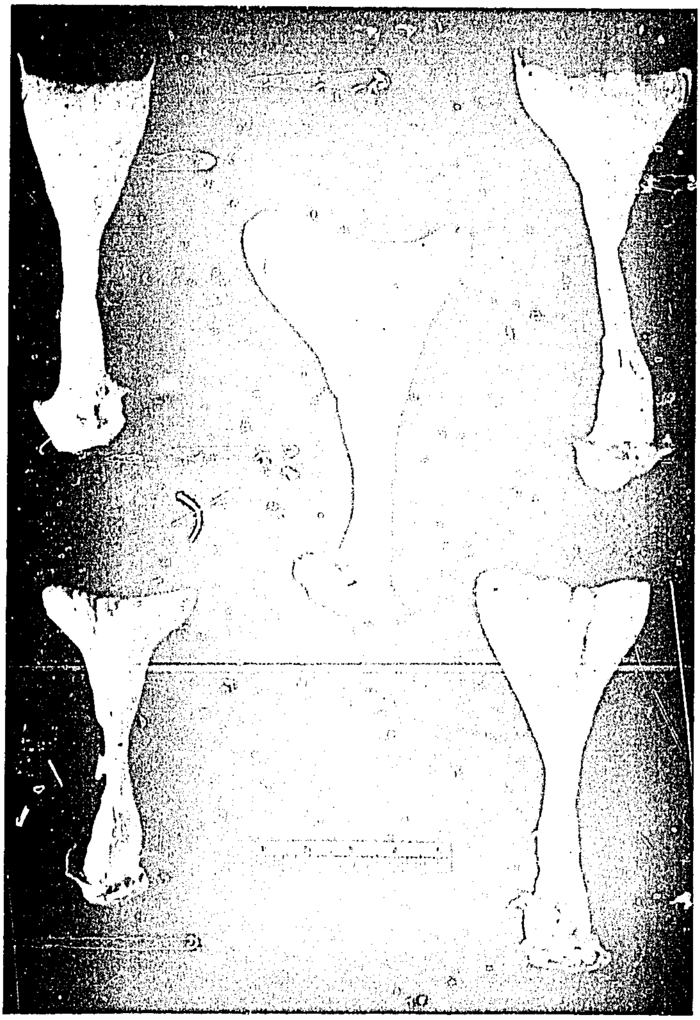

Fig. 2. Silicone rubber casts of normal, premenopausal, multiparous uteri. In two specimens note partial filling of the Fallopian tubes.

of the silicone rubber molding and plaster impression technique in relation to the intercornual dimension of freshly opened specimens was checked by direct measurement utilizing inside calipers. To afford comparative data, similar measurements were made on three representative intra-uterine devices—the large spiral, the large loop, and the stainless steel ring.

Results

As demonstrated in Figure 3, the transfundal superior and transfundal inferior measurements taken from uterine mold impressions provide a convenient graphic representation of variations in uterine cavity size. Each dot represents the point of convergence of the transfundal measurements in an individual uterine casting. The smallest and largest transfundal superior

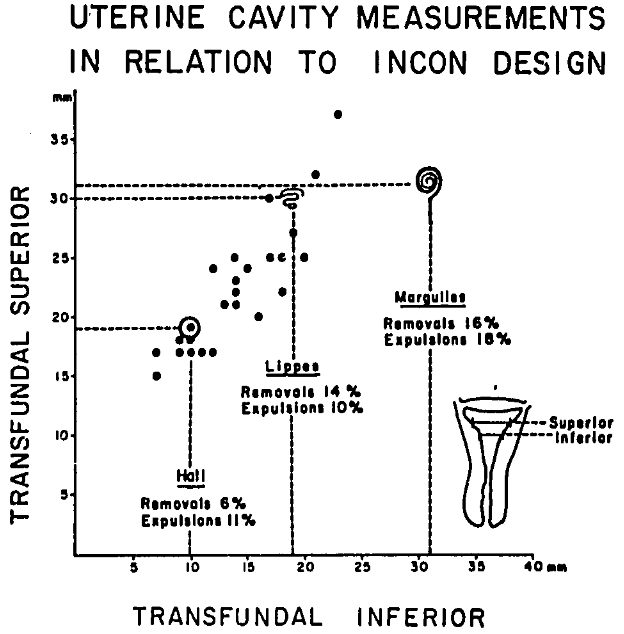

Fig. 3. Distribution graph of superior and inferior transfundal measurements in 25 normal, parous, premenopausal uteri (silicone molding technique).

measurements were 15 mm and 37 mm respectively. Values for the transfundal inferior measurement ranged between 7 and 23 mm.

The equivalent measurements on standard intra-uterine contraceptive devices are also plotted. The large Margulies spiral measures 31 mm in diameter 1 cm from the point at which the outside rim of the spiral would normally impinge on top of the fundus. If the rings of the spiral are compressed, but not allowed to overlap, the superior transfundal dimension of the Margulies spiral corresponds roughly to the dimensions of the large Lippes loop. The latter measures 30 mm at the level of the transfundal superior and 19 mm at the level of the transfundal inferior dimension. While both the Lippes loop and Margulies spiral, unless severely compressed, appear to lie outside the midrange of normal uterine dimensions as determined by this study, the plotting of the measurements for the Hall stainless steel ring gives values of 19 mm in the transfundal superior and 10 mm in the transfundal inferior dimension, placing this device at the lower end of the uterine size-distribution range.

Other measurements which were carried out on these specimens are likewise of interest, but correlate less well with the size of the endometrial cavity than the transfundal superior and inferior determinations. The complete data obtained from measurements carried out on these 25 normal premenopausal multiparous uteri are presented in Table I. Measurements of the transverse intercornual dimension, for example, range between 24 mm and 41 mm. But because of a considerable variability in the convexity or concavity of the top of the uterine cavity, and variations in the degree of bicornuality, the transverse intercornual measurement is not an accurate expression of uterine cavity size.

The range of variation in the axial dimension (the distance between the internal os and the top of the fundus) was between 30 mm and 49 mm, and this value was therefore one of the most constant of the measurements recorded. Little correlation was observed between the values recorded for the axial dimension of the uterus and actual uterine cavity capacity. Specimen No. 4, for example, which measured 49 mm in the axial dimension, measured 23 mm in the transfundal superior and 14 mm in the transfundal inferior dimension, so that it represented a long tapering cavity rather than a large cavity.

TABLE I

*Complete uterine cavity measurements in 25 studied cases**

Transfundal superior	Transfundal inferior	Intercornual dimension	Axial dimension
24	15	30	38
22	18	25	46
15	7	24	30
23	14	28	49
20	16	24	44
18	10	29	34
19	10	34	40
17	11	26	35
21	15	28	47
25	20	28	44
17	7	32	40
17	10	26	35
17	9	30	32
27	19	31	43
22	14	28	44
25	18	33	33
37	23	39	42
30	17	32	39
25	14	30	33
23	15	33	38
25	17	32	39
17	12	26	34
32	21	41	34
21	13	33	32
24	12	35	38

* Uterine cavity dimensions, in millimeters, from 25 normal, parous, premenopausal uteri. Data taken from plaster of paris impressions made from silicone uterine cavity molds. The *transfundal superior* is the transverse dimension of the uterine cavity at a distance one centimeter inferior to the top of the fundus. The *transfundal inferior* is taken at a level two centimeters inferior to the top of the fundus. The *intercornual dimension* shows considerable variability and correlates poorly with over-all fundal capacity. The *axial dimension* is the distance between the internal os and the top of the fundus.

Discussion

It is apparent that the human uterus is not a standard object with respect to size and contour. The range in transfundal measurements among these normal premenopausal parous uteri is considerable. The largest uterus in our series measured 37 mm in the transfundal superior dimension while the smallest measured only 15 mm at the same level. Of interest is a suggestive correlation between rejection rates for devices and their position on the graph. The figures for "removals" and "expulsions" for each of the three devices were summed from the *Fourth Progress Report* of the National Committee on Maternal Health.[6] It is to be noted that the spiral and the loop, with their larger transfundal measurements, appear to be rejected by the uterus (either expulsions or indicated removals) at a significantly greater rate than the smaller steel ring.

It is conceivable that to a certain extent the rejection rate of the larger intra-uterine devices could be a function of discrepancies between size of device and uterine cavity dimensions. Admittedly, it is difficult to be certain that rejections are caused solely by disparity between cavity and device. With certain of the designs, smaller versions apparently facilitate expulsion. If reducing the size of the device to correspond with observed uterine size values results in an intrinsically flimsy device, for example, then the raw figures on rejections might be expected to rise; the smaller versions of the loop and spiral do demonstrate high expulsion rates.

So long as our knowledge of mechanism of action of the INCON remains sketchy, it might be postulated that moderate distension of the uterine cavity is desirable. But there are probably limits to the degree of accommodation or distension for optimal results. Intra-uterine contraceptives are, by definition, for use within the uterine cavity. It would seem that the design characteristics of such devices should take into consideration a knowledge of the uterine morphology. The observed disparities between the measurements recorded for uterine cavity dimensions in this series of normal premenopausal multiparous uteri and comparable measurements carried out on some devices indicate that either the uterus accommodates to the device, or the device accommodates to the uterus. Whether improvement in function might result from refinement in design remains to be seen.

If consideration is given to pregnancy rates alone, the *Fourth Progress Report* of the National Committee on Maternal Health does appear to support the continued use of the larger devices. The pregnancy rates for the larger spirals and loops are indeed significantly lower than for the other intra-uterine contraceptives mentioned. The fact that their size perhaps results in better coverage of the endometrial surface might explain their success in keeping the pregnancy rate low. Unfortunately, their success is tarnished by an undesirably high incidence of bleeding complications and expulsions. It would seem reasonable to conclude that some of these complications might be avoided without necessarily sacrificing contraceptive effectiveness.

Results of this study conform to the generally accepted view of the human uterine cavity as an open envelope in the form of an isosceles triangle standing on its apex. Beyond this simple statement, it is well to note that the sides of the cavity are by no means straight lines, and that there is variation in the degree of concavity of the base of the triangle, amounting at times to a rudimentary septum.

An ideal intra-uterine contraceptive device should probably allow for the very considerable variations observed in cavity size among normal multiparous uteri. An ideal INCON should also combine two mechanically contradictory characteristics: ease of insertion and resistance to expulsion. Additionally, the ideal INCON should achieve both a low pregnancy rate and a low complication rate. None of the intra-uterine devices currently in use completely satisfy these criteria. Based on the measurements and concepts here presented, the performance of a plastic ring corresponding to the midrange of fundal dimensions, and an accommodative shield design is currently being evaluated in the Department of Gynecology and Obstetrics at The Johns Hopkins Hospital.

Summary

The resurgence of interest in intra-uterine contraception makes accurate knowledge of the dimensions of the normal human uterine cavity imperative. A series of 25 normal premenopausal parous uteri obtained via vaginal hysterectomy were used to make silicone rubber

uterine cavity casts. Plaster of paris impressions were prepared secondarily and standardized measurements secured to provide an index of uterine cavity size. Comparable measurements were simultaneously taken on three of the principal intra-uterine contraceptive devices.

The large spiral and loop devices, unless severely compressed, are observed to lie outside the size range of most uterine cavities observed, and it is noted that these large devices have a higher apparent rejection rate than the stainless steel ring. Conversely, the ring has a somewhat higher pregnancy rate, suggesting inadequate coverage of the endometrial cavity. Consideration of standardized uterine cavity measurements either in fitting or in accommodative design could lead to devices with improved characteristics.

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MILK EJECTION: A STUDY IN WOMEN USING INTRA-UTERINE DEVICES*

by

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and JUAN ZAÑARTU, M.D.**

The inhibition of milk secretion estrogens during pregnancy has long been known. This action is probably correlated with progesterone.[1,2,8] The inhibition normally ceases immediately after delivery with a decrease of these hormones in the blood stream.[5,7] It has been suggested that gestagens, which are used to inhibit ovulation as a fertility control measure, may also decrease and possibly inhibit lactation. Intra-uterine contraceptive devices, on the other hand, would not be expected to modify lactation, although, so far as we know, no experimental study has been reported on the effects on lactation of different methods used for fertility control.

In this paper we report some observations on the effects of intra-uterine contraceptive devices and a gestagen — medroxyprogesterone acetate (MPA) — on milk ejection.

Thirty-five lactating women are included in this report. Sixteen had been using the intra-uterine device described by Zipper et al.[12] for periods ranging from 3 to 377 days (Group 1). Twelve were given a single intra-muscular injection of 500 or 1,000 mg MPA between 4 and 75 days before the day of the experiment (Group 2). The action of MPA was checked by its effect on cervical mucus and/or colpocytology and/or endometrial biopsy. Seven untreated subjects served as controls (Group 3). Details of age, parity and lactation are given for the three groups in Tables I, II, and III, respectively. Where applicable, duration of use of intra-uterine devices, and gestagen dosage and response, are given for each subject.

Materials and method

The milk ejection reflex was studied by recording intra-mammary pressure by the method reported by Sica-Blanco et al.[11] (Figure 1). It is the same method as used in rabbits and other animals by several investigators.[3,4,9] Mammary contractions were produced either spontaneously, by the administration of oxytocin, or by suckling.

The oxytocin was introduced into an arm vein through a polyethylene catheter connected to a three-way stopcock through which 5 percent glucose solution flowed constantly. Different doses were diluted to a volume of one ml with 5 percent glucose solution to determine the threshold dose (in milli-units of oxytocin) and the response (in mm Hg) to increasing doses.

Spontaneous contractility

During the experiment 5 of the 16 women with the IUCD, 2 of the 7 controls, and 4 of the

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TABLE I

Record of 16 experimental subjects using intra-uterine contraceptive devices

Age (years)	Parity	Period of lactation (days)	Period of IUCD use (days)	Sensitivity to oxytocin	
				Threshold dose (milli-units)	Max. response (mm Hg)
42	7	71	7	0.125	27.0
43	4	54	14	0.25	24.0
35	7	130	5	1.00	8.5
32	6	125	3	0.25	29.0
35	11	62	6	0.50	36.0
34	6	148	4	0.25	19.0
29	4	83	40	0.50	37.5
32	5	66	17	1.50	9.0
34	8	55	4	0.50	60.0
43	4	181	147	1.50	18.5
32	8	98	30	0.25	35.5
34	5	177	82	0.50	26.0
29	6	147	67	1.00	27.0
33	11	334	270	0.75	15.5
33	7	426	377	1.00	30.0
24	4	98	57	0.75	14.5
Average: 34.0	6.4	141		0.66	26.1

TABLE II

Record of 12 experimental subjects treated with MPA

Age (years)	Parity	Period of lactation (days)	MPA					Sensitivity to oxytocin	
					Response				
			Dose (mg)	Days since treated	cervical mucus	colpo-cytology	endometrial biopsy	Threshold dose (milli-units)	Max. response (mm Hg)
28	3	111	500	10	—	—	—	1.25	30.0
29	6	234	500	35	+	+	+	1.00	19.5
24	3	295	1000	27	+	+	—	1.00	40.0
24	6	65	1000	31	+	—	—	2.00	14.0
29	6	78	500	24	+	+	—	3.00	10.5
33	9	154	500	22	—	—	—	1.50	38.0
25	4	130	500	23	—	—	—	0.75	13.25
37	11	108	1000	58	+	+	—	0.50	35.5
28	3	130	1000	37	+	+	+	1.00	14.0
30	6	220	500	68	—	—	—	1.00	18.5
34	7	55	500	4	—	—	+	0.75	15.0
35	6	200	500	75	+	+	—	0.75	9.5
Av.: 29.7	6.8	148						1.21	21.5

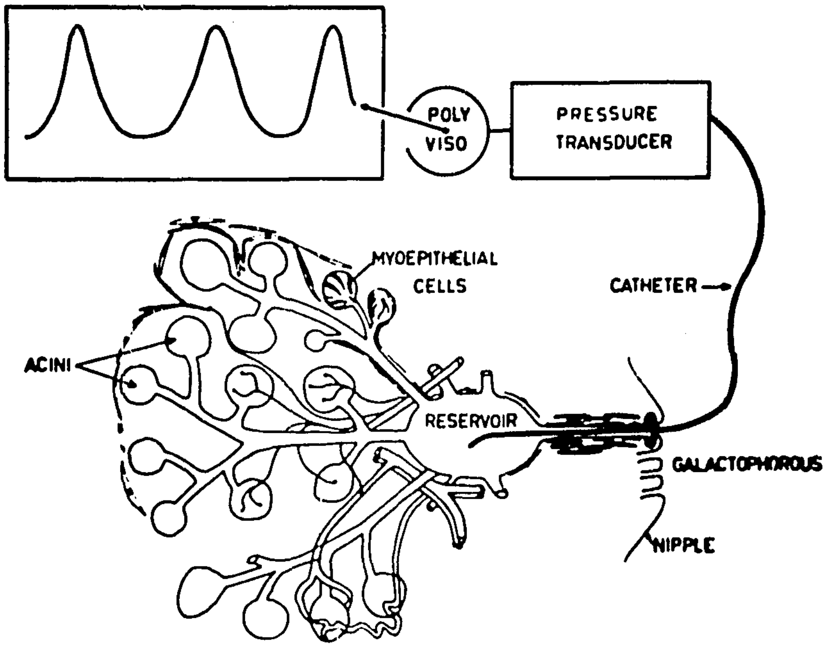

Fig. 1. Schematic illustration of the method employed for recording intramammary pressure. A thin polyethylene catheter is introduced into one mammary duct and connected to a pressure transducer. The pressure can be recorded simultaneously in several ducts of the same gland. (Reprinted by permission, from Y. Sica-Blanco *et al.*[11])

TABLE III

Record of 7 untreated experimental subjects (controls)

Age (years)	Parity	Period of lactation (days)	Sensitivity to oxytocin: Threshold dose (milli-units)	Sensitivity to oxytocin: Maximum response (mm Hg)
19	5	92	0.50	48
29	6	54	0.25	23
32	8	41	0.12	40
37	5	105	1.00	26
38	8	42	0.50	15
23	3	106	0.50	27
36	6	75	0.50	28
Average: 30.6	5.9	74	0.48	29.6

12 women treated with MPA, showed contractions of the mammary gland related neither to administration of oxytocin nor to suckling. We believe that these spontaneous contractions are due to other stimuli which we did not investigate or identify. In all groups this type of mammary contraction was observed with the same frequency, that is, in one of every three experiments.

Administration of oxytocin

As has been established in previous reports,[10] oxytocin when given intravenously in rapid injections to lactating women may produce either a single contraction of the mammary gland or a multiple wave, with two or more successive contractions, if oxytocin is administered in larger doses. To study the dose-response relationship we considered only those doses of oxytocin that produced a single contraction.

The threshold dose of oxytocin was determined for each woman. As reported by Sala,[9] a small increase in dosage above the threshold dose produces a great increment in the pressure developed by the mammary gland. Further increases in dosage produce smaller increments in pressure until a maximum response is reached. Threshold dose and maximum response for each woman are shown in Tables I, II, and III. The average threshold dose for the control group (0.48 milli-units oxytocin) is somewhat less than for the group using IUCD (0.66), but the difference is not statistically significant. The threshold dose for the group treated with MPA (1.21) however, is significantly greater than for the other two groups.

There is no significant difference between the three groups in maximum response.

Milk ejection reflex to suckling

The effect of suckling on mammary contractility was recorded in all subjects. In the three groups the pattern of response was similar: a few seconds after the baby started suckling, the mammary gland began to contract rhythmically, these contractions persisting until suckling ended. The initial contraction was always the greatest, and was equivalent to the maximum possible response.

The same pattern of reaction to suckling was observed in patients treated with MPA, with the exception of three cases in which suckling produced a minimal response. We did not find any explanation for these exceptions.

Summary

Mammary contractility was studied in 35 women by recording intralobular pressure variations, using the method described by Sica-Blanco.[11] A thin polyethylene catheter was introduced into a mammary duct. Subjects were divided into three groups: (1) women with intra-uterine devices; (2) women treated with medroxy-progesterone acetate (MPA); and (3) a control group without IUCD or MPA. On each patient the following studies were performed: (*a*) spontaneous contractility; (*b*) oxytocin sensitivity (threshold dose and maximal response to larger doses); and (*c*) milk ejection response to suckling.

No significant differences were observed between groups 1 and 3. Spontaneous contractility was similar in all three groups. The amount of oxytocin required to produce a minimum response (threshold dose) was significantly less in groups 1 and 3 than in group 2. The average maximal response was 29.5 mm Hg in the controls, 26.06 in the group using intra-uterine devices, and 21.47 in that receiving MPA. This was not a significant difference.

Despite the fact that lactation as a whole apparently was not inhibited by MPA, in three of twelve patients suckling was unable to elicit the milk ejection response in the catheterized duct.

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EFFECT OF INTRA-UTERINE DEVICES ON THE NORMAL MENSTRUAL CYCLE

by

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The Margulies spiral was placed in 60 women and an evaluation of their menstrual cycles was initiated. The patients varied in age between 16 and 41 years; 43 were between 20 and 29 years of age. Thirty-six patients were Negroes and 24 where white. Before being admitted to the study these 60 women together had 251 pregnancies, of which 39 miscarried. This was a group of proven fertility whose clinic histories suggested regular ovulatory menstrual cycles. Following the use of this device we intend to evaluate the Lippes loop, Birnberg bow, and the Stone-Hall ring for their respective effects on the normal menstrual cycle.

We chose the following parameters to evaluate the menstrual cycle. Follicle stimulating hormone (FSH) and luteinizing hormone (LH) were measured throughout the menstrual cycle. Urinary estrogens and pregnandiol were also done throughout the cycle. Vaginal smears by the Shorr method were done in both the proliferative and secretory phases of the menstrual cycle. Vaginal cytology was used to establish the endocrine pattern of the menstrual cycle in which an intra-uterine device (IUCD) was in place. Endometrial aspirations were also taken in the proliferative and secretory phase of the menstrual cycle. Endometrial cytology was done to determine the endocrine pattern found on a specific day of the menstrual cycle with the IUCD in place. Along with the endocrine pattern of the endometrium, the aspirations were also screened for evidence of infection or inflammation due to the intra-uterine device. These aspirations were felt to be a simple way to diagnose endometritis if such existed. To further evaluate the endometrium histochemistry studies were undertaken. The endometrial specimens were obtained by either curettage or from hysterectomy specimens. Endometrial tissue was taken in both the proliferative and secretory phases of the menstrual cycle from patients who had the intra-uterine device in place. It was felt that a careful correlation of FSH, LH, urinary estrogens, pregnandiols, vaginal smears, endometrial cytology and histochemistry would point up any obvious alterations in the menstrual cycle due to the intra-uterine device.

Gonadotropins and steroids

The first parameter studied was the effect of the Margulies spiral 5 on FSH and LH throughout the menstrual cycle. Figure 1 demonstrates FSH and LH values throughout the normal menstrual cycle. FSH is measured by the Steelman-Pohley assay and LH by the ascorbic acid depletion assay of Parlow. FSH is found high during menstruation and immediately post-menstrual. It is at its lowest point at mid-cycle, being in a reciprocal relationship with endogenous estrogen. It again rises pre-menstrually as corpus luteum estrogen wanes. LH, however, is characterized by a solitary peak at the time of ovulation and is otherwise unmeasurable throughout the menstrual cycle.

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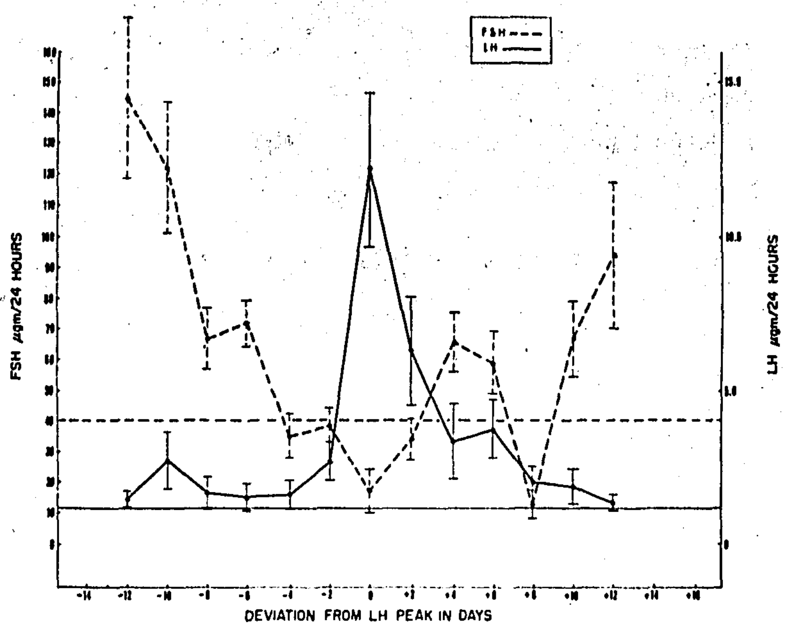

Fig. 1. FSH and LH throughout the normal menstrual cycle.

Two patients were studied for serial FSH and LH who had the Margulies spiral in place. The FSH and LH assays were performed in an identical manner to those in the composite cycle, but the gonadotropin extraction procedure was modified. Instead of the kaolin-acetone technique a tannic acid extraction was used and the LH precipitate was further purified with celite. This might account for the higher values of FSH and LH which were found in IUCD cycles.

Patient B had a Margulies spiral 5 in place for three months. She had a 22-day cycle and the FSH values deviated from those seen in the normal cycle. We had the highest values of FSH post-menstrual that we have ever recorded. They were of the magnitude of 424, 276 and 256, when we usually see a range of 160 to 180 μg. of NIH-FSH standard. FSH in this cycle was at its lowest point at ovulation but returned to higher levels pre-menstrual. In patient H, who had the coil in for five months, FSH was again extremely high post-menstrual and also pre-menstrual. Again the NIH-FSH μg./24 hours was 256, 280, 376 post-menstrual and the same order of magnitude pre-menstrual (Figures 2, 3).

Both patient B and H had a different LH peak than that seen in the normal menstrual cycle. Patient B had the highest LH peaks we have ever seen, being 56 and 44 μg. NIH-LH/24 hours. This peak was also broad, lasting six days. In patient H the LH peak was at 10 μg. NIH-LH/24 hours by day ten. We commonly associate LH levels of 10 μg. with ovulation and such was the case here. However, instead of a solitary two-day peak of LH, the LH values remained at 10 μg. for the remainder of the cycle (Figures 2, 3).

In the two cycles studied we therefore had short cycles and quantitative differences in both FSH and LH. Whether this is due to the intra-uterine device or to the altered extraction technique is not currently known. These patients both ovulated, had an altered mid-cycle LH peak, and had the same general distribution of FSH post and pre-menstrually. The alteration, particularly of FSH, was one of magnitude.

Urinary estrogens E_1, E_2, E_3 and pregnandiol were done on these two patients. The tannic

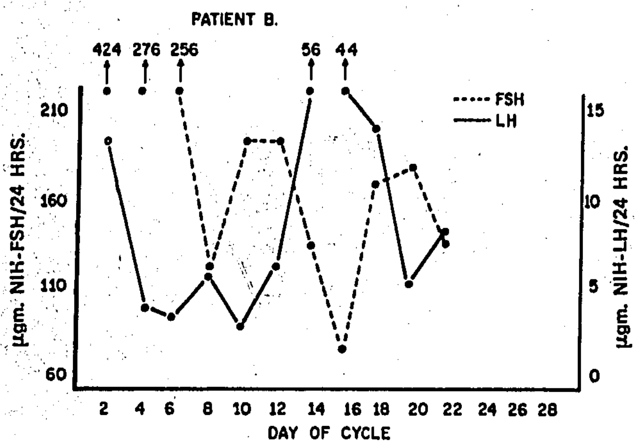

Fig. 2. FSH and LH in patient B, who had a Margulies spiral 5 in place for three months.

acid extraction affected the hydrolysis of the urinary conjugates accounting for the low values of both urinary estrogen and pregnandiol. Since this represents a preliminary report on these studies, similar cycles for FSH and LH must be done with kaolin and acetone extraction. The urinary estrogens and pregnandiols will be repeated and re-correlated with the FSH and LH data. It is our impression that for the most part these cycles are ovulatory but it remains for us to prove whether there is a state of hyperestrogenism and/or whether the corpus luteum phase is altered.

Vaginal and endometrial cytology

In the evaluation of an intra-uterine contraceptive device such as the Margulies spiral 5, the influence of the foreign body on the endometrium itself seems of prime importance. A possible influence could be either direct in the form of irritation or infection, or indirect, by changing the endocrine balance and thus rendering the endometrium the anovulatory type instead of the normal cyclic pattern.

It would seem that the study of possible irritation of the endometrium can best be performed on the endometrium itself. This can be accomplished by study of the endometrial biopsy or of the endometrial aspiration. The endometrial aspiration has proven to be a reliable indicator of irritation, endometritis, and premalignant changes in the endometrium[1]. Previous studies have shown that endometrial cytology can also be used to evaluate cyclical changes in the endometrium[2]. The morphology of the cytologic pattern will indicate whether the endometrium is in the early or late proliferative, or in the early or late secretory phase.

The study of an endometrial intracavitary aspiration will thus give information on both the direct and indirect influence of the IUCD on the endometrium. Although less accurate than the study of the endometrial biopsy, the advantage is that such an aspiration can be obtained without discomfort to the patient and without disrupting the cyclical events. An endometrial biopsy creates a wound in the endometrium, with subsequent healing efforts, which disturbs the pattern found in a subsequent biopsy. Intracavitary aspiration, however, does not disturb the existing pattern.

Vaginal endocrine cytology may give an impression of an existing endometritis and cervicitis, and shows a vaginitis, if present. The main goal of the study of the vaginal cell pattern,

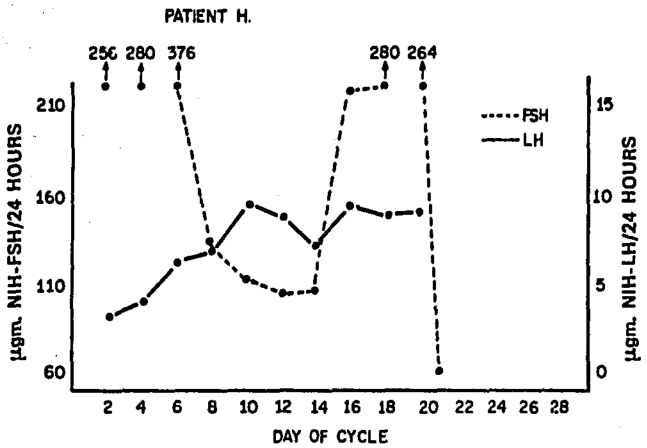

Fig. 3. FSH and LH in patient H, who had a Margulies spiral 5 in place for five months.

however, is to evaluate the cyclic changes, date the cycle, and detect eventual deviations from the normal cycle[3]. It is of great value correlated with the endometrial samples.

Before a spiral was inserted, a vaginal smear and an endometrial aspiration were taken. The vaginal smear was obtained from the upper part of the lateral wall of the vagina, where cervical contamination was purposely avoided. The endometrial aspiration was taken with a thin rubber catheter, inserted through the cervix into the endometrial cavity. The slides were placed in a fixative consisting of equal parts absolute alcohol and ether. The vaginal smears were stained with the Harris-Shorr staining technique. Two slides were prepared of each of the endometrial samples. One of these was stained with the Harris-Shorr staining technique, the other one with the Papanicolaou staining procedure. During each return visit a repeat vaginal smear and endometrial aspiration was obtained. In a few cases this procedure was omitted. In 149 patient visits a total of 138 endometrial aspirations were obtained and 130 vaginal smears.

Vaginal smears

Of the 130 vaginal smears, 3 were dried out and inadequate for interpretation. Of the remaining 127, 57 were obtained during the patient's first visit, prior to the insertion of the IUCD. There were 41 smears taken during the first return visit, 25 during the second return visit and 4 during the third return visit.

Of the 127 smears, 73 could be classified as pre-ovulatory smears and 48 as postovulatory smear patterns. A pre-ovulatory smear pattern implies that only estrogen effect on the vaginal epithelium is mirrored in the smear. This causes a picture of cells exfoliated from the intermediate and superficial layers of the vaginal epithelium. A moderate estrogen stimulus will cause exfoliation of mostly intermediate cells, while a stronger estrogen stimulus will produce predominantly superficial cells. In a normal cycle the estrogen stimulus from the graafian follicle will increase steadily from the beginning of the cycle until ovulation. Intermediate cells are basophilic, stain blue with the Harris-Shorr staining technique, and have vesicular nuclei; superficial cells are acidophilic, stain red with the technique, and have pyknotic nuclei. Pyknotic nuclei are black, punctiform and have a diameter not exceeding 6 microns. The background of the smear showing estrogen effect will be essentially clean in the absence of infection. The cells will be found separate from each other, without clumping.

A postovulatory smear pattern is characterized by the predominance of intermediate cells, which blend together in clusters without visible cell boundaries, the so-called "placards". The background is filled with Döderlein bacteria. The number of superficial cells which were present at the time of ovulation will steadily decrease during the postovulatory phase, while the number of placards increases, until the 26th day of the cycle. Between the 26th and 28th day an increase in superficial cells is found, and the number of placards is decreased. This cell pattern constitutes the premenstrual smear.

There were 6 smears which could not be classified as either pre- or postovulatory smears, because they did not show a pattern consistent with a normal cycle day. These smears showed either extreme cytolysis, an exaggerated and prolonged estrogen effect, or the presence of pregnancy cells.

When the vaginal smears were compared with the actual day in the cycle of the patient, it was found that 104 smears were compatible with the actual day of the cycle, while 23 were incompatible with the actual date. Incompatibility with the day of the cycle may mean either a pre-ovulatory smear type in the second half of the patient's cycle, or an obviously insufficient estrogen effect close to the time of ovulation. It was also observed that 8 of these abnormal smears were found in the group of the 57 control smears, taken prior to the insertion of the IUCD. Two of these cases could be explained by previous administration of ovulation-suppressing drugs. Two other cases could be followed through two consecutive anovulatory cycles. In one the short time interval since the last delivery was probably responsible for the anovulation. Table I shows the distribution of the smear types with regard to the time of the cycle in patients with the IUCD in place.

TABLE I

Vaginal Smears	Number
Number of cases	138
Inadequate samples	11
Total number evaluated	127
Pre-ovulatory	73
Postovulatory	48
Abnormal smears	6
Smears compatible with the cycle day	104
Smears incompatible with the cycle day	23
57 original visits—compatible	49
incompatible	8
41 first returns—compatible	29
incompatible	12
25 second returns—compatible	22
incompatible	3
4 third returns—compatible	4

Endometrial aspirations

These were evaluated both for endocrine effect and for the presence of inflammation. As described in a previous article, we found endometrial cytology not an adequate means of dating a cycle with the same accuracy as from the study of endometrial biopsies. However, an endometrial smear can be classified as a proliferative or a secretory smear. The nuclei in the cells from the proliferative phase have a chromatin pattern which is much finer and lighter than that in the nuclei of cells in the secretory phase, which generally show a clumped and darker chromatin pattern. While the nuclei in the proliferative phase are usually uniform in size and shape, during the secretory phase a large variety of shapes and sizes are found in the nuclei. Also the nucleoli are generally much more outstanding and more numerous in the secretory than in the proliferative phase. It should be emphasized that we use only the glandular cells for our evaluation, and do not evaluate the stromal cells, which are simultaneously present in the smears.

The 8 smears that were labeled "abnormal" showed either abnormal cell types or had the characteristics of the smear type such as found in cases of cystic glandular hyperplasia of the endometrium.

Table II shows the distribution of these smears with regard to the groups with the IUCD remaining *in situ* and the IUCD removed, respectively. It is of interest that the relative number of inadequate samples is much larger in the group with the IUCD remaining *in situ* than in the "problem" group, in which the IUCD had to be removed.

TABLE II

	Group I IUCD in	Group II IUCD removed	Total
Not enough cells	25	5	30
Anovulatory	2	6	8
Proliferative	44	25	69
Secretory	21	10	31
	92	46	138

When the endometrial aspiration smears were compared with the vaginal smears, a complete correlation was found in all cases where both were available for evaluation. However, it should be noted that in cases where the vaginal smear indicated the beginning of progesterone effect, such as immediately after ovulation, the endometrial aspiration still had the characteristics of a late proliferative smear. This is due to the more sluggish reaction of the endometrium to progesterone effect, as compared to the vaginal epithelium.

Inflammation

An endometrial smear can be evaluated for signs of inflammation. The presence of leukocytes has to be carefully evaluated. Leukocytes that do not intermingle with the endometrial cells, but rather are found in mucous strings or lying in clusters in separate foci, may very well originate from the endocervix and be inadvertently aspirated with the intra-uterine contents. The presence of these leukocytes thus does not necessarily implicate the endometrium.

However, if leukocytes are found dispersed diffusely through the entire smear and actually interspersed between the endometrial cells, their source is most likely the endometrium. During a normal cycle, leukocytes are normally found in the endometrium premenstrually and during the menses. At any other time their presence usually signifies actual infection, and means the presence of an endometritis. The other possibility, namely necrosis from pressure of the intra-uterine device on the endometrium, is less likely in view of the fact that necrosis without infection, such as in cases of necrotic polyps or necrotic leiomyomata, usually does not cause the appearance of leukocytes in the endometrium. However, only bacteriological studies can indicate whether or not an actual infection is present.

The presence of "abnormal" cells can also only be recorded without stating an opinion on whether or not their presence is caused by an actual infection or from necrosis. The cells we classified as "abnormal" had either vacuolation of the cytoplasm or irregularly shaped hyperchromatic nuclei, or both.

We attempted to divide the degrees of inflammation into three groups. In Group I were placed the smears with leukocytic reaction only, in Group II the smears that showed a predominance of leukocytes, with endometrial cells scattered in between, and in Group III we placed the smears with leukocytic reaction plus the presence of abnormal glandular endometrial cells. Clinically we interpreted the smears as follows: In the first group due to the nature of the material we reserved opinion on whether the leukocytes derived from the cervix or the endometrium. In the second group we felt that there was evidence of endometrial inflammation. The third group represented a frank endometritis. In two cases of this third group, in which a curettage was performed, the histologic diagnosis was acute endometritis. Although we did not find plasma cells in our smears, they were present in the curettings.

In 36 endometrial aspirations signs of inflammation were found. Of these, 18 belonged in the first group, 6 in the second group, and 12 in the third group. In one case, the inflammation was found in the smear taken prior to the insertion of the IUCD, and curettage showed acute endometritis. In one case a missed abortion was diagnosed from the vaginal smear and the endometrial aspiration. Table III shows the distribution of these three groups of smears with regard to the return visits.

TABLE III

	Patients	Group I	Group II	Group III	Total
1st clinic visit	60	0	0	1 (1)	1 (1)
2nd clinic visit	53	9 (5)	2 (0)	3 (0)	14 (5)
3rd clinic visit	30	7 (0)	3 (3)	6 (2)	16 (5)
4th clinic visit	6	2 (2)	1 (1)	2 (1)	5 (4)
	60	18 (7)	6 (4)	12 (4)	36 (15)

The figures in parentheses signify the number of coils which had to be removed.

Group I comprises 13 patients who had 18 smears with leukocytes present. Seven of these 13 patients had the coil removed for either bleeding, pain, or miscellaneous symptoms. Group II represents 6 endometrial aspirations in 4 patients whose smears revealed leukocytes scattered among endometrial glandular cells. All 4 patients required removal of the coil because of patients' complaints. The third group includes 8 patients with abnormal endometrial cells and leukocytes. Four of the 8 patients had the coil removed when this interim study was concluded. The remaining 4 patients had the coil removed at a later date for patients' complaints. All Group II and III patients required coil removal, while 7 of the 13 patients in Group I had the coil removed. The Margulies spiral with cervical appendage caused a large incidence of endometrial reaction and/or inflammation and in some instances frank endometritis. The preliminary work with the Lippes loop suggests a great reduction in this problem.

In a previous publication[4] the histochemical observations in the endometrium were described during each day of the normal menstrual cycle utilizing a battery of histochemical techniques. Alkaline phosphatase, beta glucuronidase, ribonucleic acid (RNA), succinic dehydrogenase (SDH), triphosphopyridine nucleotide (TPNH), and non-specific esterase were present in strong concentrations during the proliferative phase and in decreased concentrations during the secretory phase of the cycle. Conversely, acid phosphatase, lactic dehydrogenase (LDH), disphosphopyridine nucleotide (DPNH), glycogen, mucin and lipids were noted in weak concentrations during the proliferative phase and in high concentrations during the secretory phase. The reader is referred to the original publication[4] for specific localizations of these histochemically reactive materials. In a general way, enzymatic activity was located principally in the cycloplasm of glandular and surface epithelia and in the walls of smaller arterioles.

In the present study, three patients wearing the IUCD were subjected to histochemical evaluation. One was in the proliferative phase and two were in the secretory phase of the menstrual cycle. The histochemical observations are tabulated in Tables IV and V. During the proliferative phase of the cycle an increase of histochemically reactive material was noted with alkaline phosphatase, beta glucuronidase, SDH, TPNH and non-specific esterase. These materials showed relatively decreased activity during the secretory phase of the cycle. Conversely acid phosphatase, LDH, DPNH, mucin and lipids were present in weaker concentrations during the proliferative phase and in stronger concentrations during the secretory phase of the cycle. The location of these histochemically reactive materials is noted in Tables IV and V, with concentrations estimated semi-quantitatively as + to 4+. Trace amounts are designated as ± and strong concentrations as 4+.

TABLE IV

Proliferative endometrium

Histochemical reaction	Gland	Gland lumen	Vessel	Stroma
Alkaline phosphatase	++	—	++	±
Acid phosphatase	±	—	±	±
Beta glucuronidase	+++	—	++	+
LDH	+	—	+	±
SDH	+++	±	+++	+
DPNH	++	±	+	
TPNH	++++	±	+++	
Periodic acid Schiff	±	±	±	±
Mucin	±	±	±	±
DNA	+	—	+	+
RNA	++	—	+	+
Lipids	+	—	—	+
Esterase	++	—	+	++

From the above histochemical observations we may conclude that there are no appreciable differences in histochemical activity between endometria of patients wearing the IUCD and those described in a previously published report which may be used as a control group. Therefore, it appears that the presence of an IUCD has no appreciable effect on endometrial enzyme activity or other histochemically reactive materials based on three patients studied in this group. It should be noted that there was no appreciable infection in these three patients.

At the present time there has been no attempt made to study myometrial changes occurring in patients wearing the IUCD for a prolonged period of time. Of particular interest would be the connective tissue changes around blood vessels and between muscle bundles of the myometrium and cervix.

TABLE V

Secretory endometrium

Histochemical reaction	Gland	Gland lumen	Vessel	Stroma
Alkaline phosphatase	+	+++	+++	±
Acid phosphatase	++	++	+	+
Beta glucuronidase	+	—	+	±
LDH	++++	—	+++	++
SDH	+	±	++	±
DPNH	++++	±	+++	++
TPNH	++	—	++	+
Periodic acid Schiff	+	+++	±	±
Mucin	+	++	±	±
DNA	+	—	+	+
RNA	+	—	+	+
Lipids	++	—	—	++
Esterase	++	—	+	++

Summary

1. Clinical data indicate that the menstrual cycle is short the first two or three months the IUCD is in place. After this period of time the cycles generally resume their normal length.

2. FSH and LH data suggest normal ovulatory cycles with only a quantitative difference in FSH and LH secretion. There is a pronounced increase in FSH elaboration when compared to the normal menstrual cycle. This needs to be further correlated with urinary estrogen determinations. The LH values also differed from the normal menstrual cycle, but only in magnitude and length of LH elaboration.

3. Vaginal and endometrial smears indicated that ovulatory cycles occur in the vast majority of patients. The vaginal smears in particular are a practical method to ascertain whether or not ovulation takes place in these patients.

4. Endometrial aspirations proved to be an efficient way to evaluate inflammation of the endometrium. Patients who had no pain, discharge, or bleeding often had insufficient secretions for endometrial aspiration. Patients who had complications had sufficient secretions for aspiration. Once their endometrial smear was classified as belonging to Group II or III invariably the coil came out. Half of the patients who had smears in Group I had the coil removed. All patients who showed evidence of inflammation by endometrial smear continued to do so, and some of the patients were followed from smears in Group I to smears in Group III. The endometrial smears are a practical way to diagnose endometrial inflammation. It is believed that private patients with a coil in place can be followed and evaluated by endometrial aspirations. This has some obvious advantages over endometrial biopsy and D & C. It cannot replace bacteriologic studies.

5. Endometrial histochemistry studies showed no changes from the previously reported

normal menstrual cycle. In a number of instances endometrial histology was used to confirm the cytologic diagnosis of endometritis.

6. In general the endocrine evidence points to normal ovulatory menstrual cycles with the IUCD in place. The presence of hyperestrogenism, which could affect ovum transport, is yet to be proven or disproven.

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VAGINAL CYTOLOGY IN WOMEN USING INTRA-UTERINE DEVICES

by

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The contraceptive method utilizing an intra-uterine device is the most popular of all methods used in Hong Kong. Within a period of 15 months (June 1963 to August 1964) 4,048 women were fitted with it. The device used was either a Margulies spiral or a Lippes loop. A study on the vaginal cytology was instituted to determine whether the device would cause any of the following conditions: (1) carcinoma of the genital tract; (2) infection of the genital tract; (3) disturbance of ovarian cycles.

1. *Carcinoma of the genital tract*

Smears on slides were prepared by aspiration from the posterior fornix as well as by Ayre's method of scraping the portio vaginalis using Papanicolaou's technique of staining and methods of reporting. The results were then interpreted as negative or positive.

Of the smears taken from 516 consecutive patients before the insertion of the device, there was one positive case, which was later proved to be carcinoma *in situ* of the cervix and excluded from the study.

Of the repeated smears taken 9 months after the insertion of the device there was another positive case which was also proved to be carcinoma *in situ* of the cervix. The device used in this patient was a Lippes loop which was placed entirely within the uterine cavity. Since the endometrium in this case was normal and the carcinoma was found in the cervix, it is not likely that the device was the cause of it.

Although up to now the device has not been proved to be carcinogenic, the time interval (9 months after insertion) in this study is too short to be considered conclusive. It is intended to continue this study as long as this group of patients continues using the device.

2. *Infection of the genital tract*

Forty-four patients were investigated in this series. The smears were taken by aspiration of the posterior fornix in the first half of the menstrual cycle before insertion and nine months after insertion of the device. Eight patients were excluded because the pre-insertion smears showed inflammatory changes with many polymorphs, histocytes and endocervical cells. In the remaining 36 patients the pre-insertion smears showed normal patterns of the proliferative phase of the cycle. Though there was no history of pelvic infection nor increase of vaginal discharge, 13 post-insertion smears showed numerous polymorphs and histocytes. One showed isolated inflammatory endometrial cells. The remaining 23 post-insertion smears were normal and similar to the pre-insertion smears. Thus the incidence of infected smears was 36 percent. It is possible that this relatively mild local infection could have been caused by the device. A study of the pH of the vaginal fluid in cases with infected smears is now in progress.

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3. *Disturbance of ovarian cycles*

A hormonal study was carried out in 30 cases nine months after they had been fitted with the device. In each patient, one smear was taken in the first half and 3 to 5 smears (more required to detect late ovulations) in the second half of the same cycle.

Six patients had to be excluded because it was not possible to interpret the results of the smears due to the presence of numerous inflammatory cells. Of the remaining 24, there was no ovulation in 5 and smears of the remaining 19 showed ovulation as indicated by the rise of "cornification index." Thus the ovulation rate was 88 percent, which would be 96 percent if the subsequent cycle were included, as ovulation occurred in 4 of the 5 women with anovulatory cycles in the previous month. Since an anovulatory cycle may occur periodically even in fertile women without any protection it may be said that the contraceptive action of the device is not through the disturbance of ovarian cycles.

Conclusions

With due regard to the short period of study, it appears that:

1. There does not seem to be any disturbance in the ovarian cycles nor are the devices carcinogenic.
2. The use of intra-uterine devices probably causes mild localized inflammatory changes in some women.

STUDIES OF THE ENDOMETRIUM IN PATIENTS USING INTRA-UTERINE CONTRACEPTIVE DEVICES
I: HISTOLOGIC CHANGES IN THE UTERUS

by

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Introduction

The majority of studies of the intra-uterine device have indicated that few, if any, significant tissue reactions occur as a consequence of long-term use[4–8, 10, 11]. Further confirmation has been presented at this conference in the reports of Hall *et al.* and Sujan and Virick. Reports of chronic endometritis, using the traditionally accepted histological criteria, have been few, and for the most part are limited to isolated case reports,[13, 15] among which should be included the paper published herein (page 235), by Tamada and Maruyama. In contrast to these infrequent reports, several large series (reported at this conference by Tietze and Lewit, Hsu *et al.*, Satterthwaite, Williams, and Zipper *et al.*) have shown that symptomatic pelvic inflammatory disease, including endometritis and parametritis, has been diagnosed clinically in from 0.3 to 1.7 percent of women using the intra-uterine device. Although the incidence of pelvic inflammatory disease in comparable control patients of the same socio-economic ethnic groups is not known, it seems evident that symptomatic pelvic inflammatory disease occurs in a small but constant percentage of women using the intra-uterine device.

Thus, an apparent discrepancy exists between the rare reports of cases demonstrating histological endometritis using the classically accepted criteria for this diagnosis, and the reported incidence of clinical infection. In an attempt to clarify this problem, a re-evaluation of the commonly accepted histologic criteria for bacterial infection or sterile tissue reaction of the endometrium was undertaken.

Materials and methods

In order to determine the histologic changes that occur in association with the placement of the intra-uterine device in the uterus, material was obtained from two groups of patients. The first group of 21 women had Lippes loops inserted in order to prevent pregnancy. At various time intervals after insertion, endometrial biopsies were obtained. In this group the mean age was 28 years, with a range of 15 to 44 years, and all women had delivered at least one living child, with a mean of four live children. Biopsies were performed at the first follow-up clinic visit after insertion of the loop. All patients except one had at least one menstrual period between biopsy and the time of insertion. The one exception had expelled the loop two days after insertion, and had the biopsy performed five days after expulsion.

The second group of eight patients had the Lippes loop inserted prior to an elective vaginal hysterectomy in association with colporrhaphy for functional disorders such as stress incontinence. In this group, it was possible to examine the myometrium as well as the

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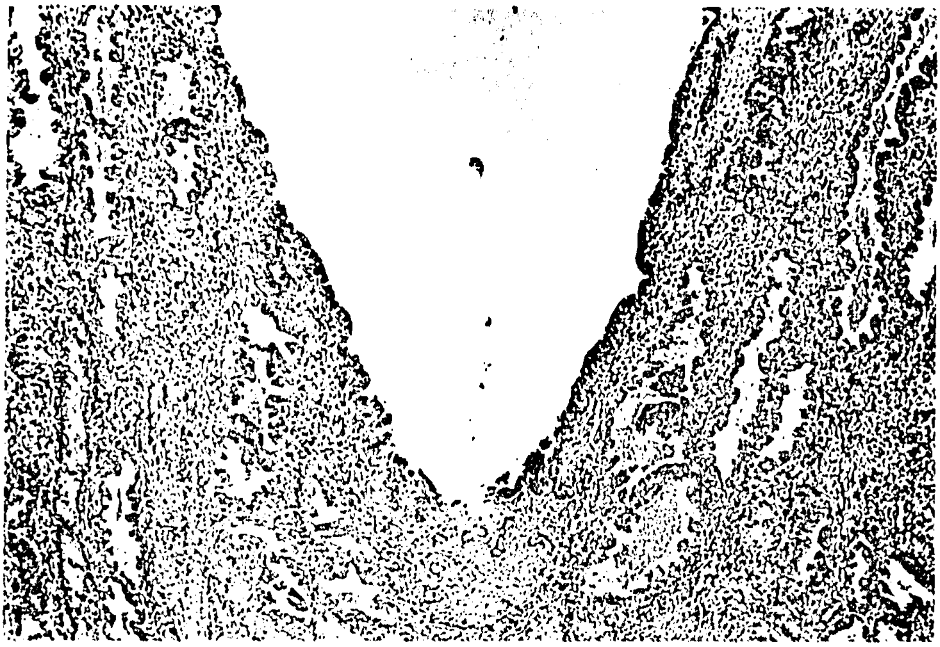

Fig. 1. V-shaped depression in progestational endometrium resulting from placement of the loop. There is minimal distortion of tissue and no evidence of ulceration. Magnification ×32.

endometrium. This group of patients had a mean age of 33 years and had delivered a mean of seven live-born children. The hysterectomies were performed at intervals of from two to 30 days after insertion of the loop. Six patients had one menstrual period between time of insertion of the loop and the hysterectomy, while two had none. In both groups none of the patients had signs or symptoms of pelvic inflammatory disease such as fever or lower abdominal tenderness. Two patients complained of leukorrhea; however, this was mild and clinically appeared to be vaginitis without cervical discharge or tenderness.

Results

Macroscopic examination of the eight hysterectomy specimens showed that the loop caused a depression of the endometrial surface without ulceration or necrosis (Figure 1). In the areas of endometrium located between the loops of the ring, focal irregular areas of recent hemorrhage and congestion of superficial endometrium were present.

In the histologic examination of the eight hysterectomy and 21 biopsy specimens, several abnormal conditions were found. It was possible to classify these changes into three descriptive categories: chronic endometritis, with or without involvement of the myometrium (Figures 5 and 6); stromal lymphocytosis (Figures 3 and 4); and subepithelial leukocytic accumulation (Figure 2). Three hysterectomy specimens showed evidence of chronic endometritis, and in two of these uteri the myometrium and even foci of adenomyosis were also involved with inflammatory cells. The histologic findings consisted of diffuse infiltrations of lymphocytes throughout the stroma, purulent intraglandular exudates, and leukocytes and plasma cells present in amounts ranging from 0 to 15 per high-power field. Stromal lymphocytosis was noted in both endometrial biopsies and in the hysterectomy specimens. The histological

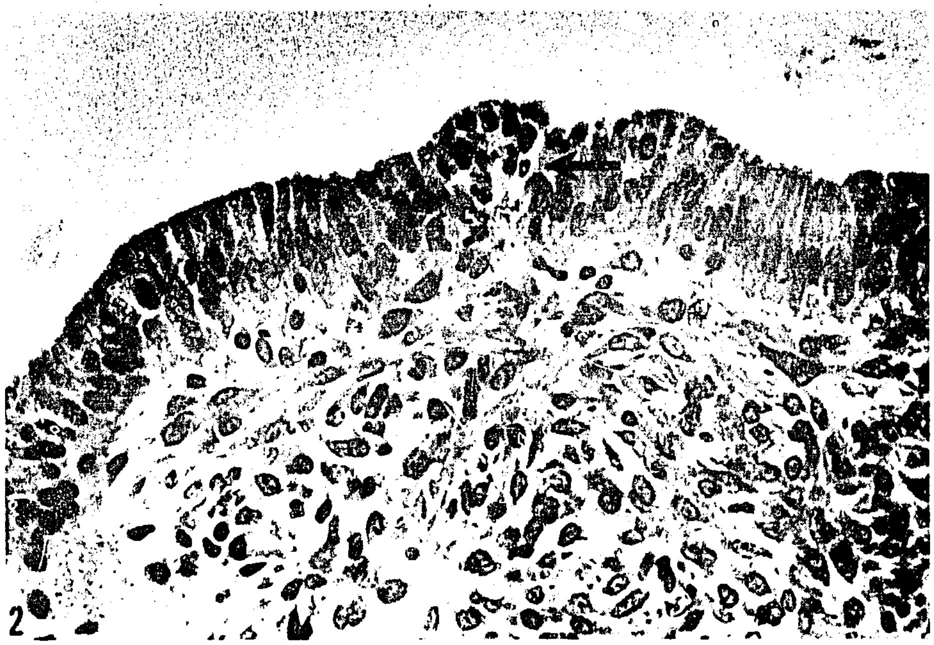

Fig. 2. Polymorphonuclear leukocytes (←) located in and beneath the superficial endometrial epithelium. Magnification ×440.

findings consisted of scattered accumulations of leukocytes, with or without lymphoid follicles, throughout the endometrial stroma. Subepithelial leukocytosis existed when occasional scattered leukocytes were present beneath the superficial epithelium of the endometrium. Rarely, the leukocytes extended down to the most superficial vessels and glands in the contiguous stroma, and occasionally lymphocytes were present in addition to the leukocytes (2 biopsies). In several biopsies of progestational endometrium, it appeared that the glands were inspissated with greater stagnation of secretions than was present in endometrium of a comparable menstrual phase obtained from patients who did not have intra-uterine devices. A 1.2 cm diameter stromaloma was present in one of the hysterectomy specimens and should be considered a coincidental finding at this time. Distribution of the uterine pathology in the two patient groups is summarized in Table I.

Discussion

It is a general biological principle that whenever a foreign material is inserted into the human body, biochemical and other tissue reactions are elicited to dispose of it. These reactions vary in their severity and appear to be related in part to the type of material which forms the foreign body. Thus, silk and catgut sutures, contact lenses, and silver clips produce different degrees of reaction in the tissues surrounding them. The silver used in the Gräfenberg ring produced a tissue reaction which was severe enough to warrant its discontinuance as a practical contraceptive device. Even though the newer plastics currently used in the manufacture of intra-uterine devices are much less reactive, they are foreign bodies nevertheless, and as such produce a tissue reaction in the human body. Evaluation of the foreign body tissue reaction produced in the female genital tract, particularly the endometrium, is complicated because the presence of inflammatory cells in the endometrium is a normal physio-

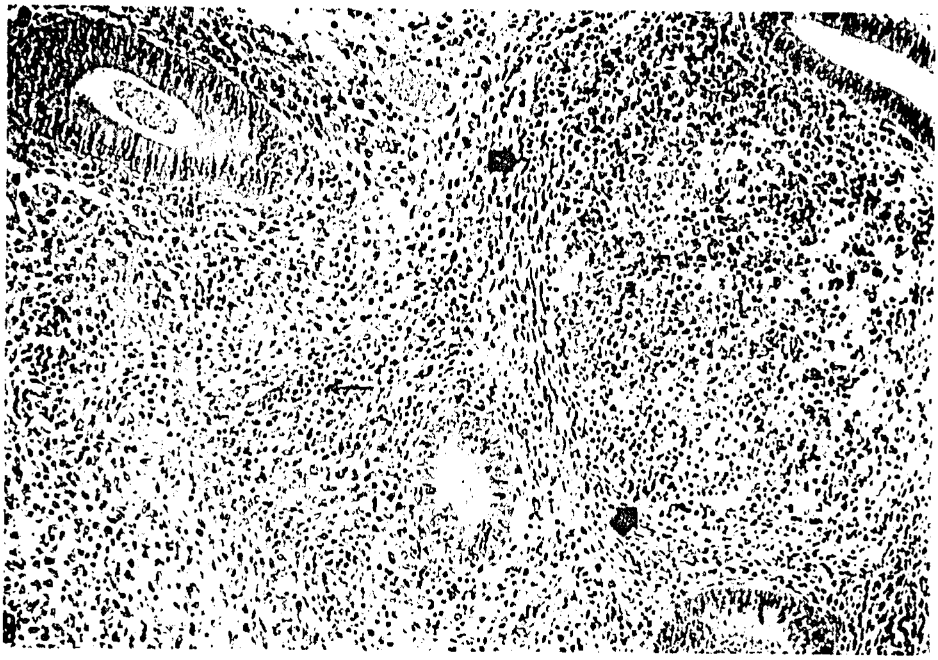

Fig. 3. Lymphocytes (<—) diffusely scattered in endometrial stroma and a lymphoid follicle (—>). Magnification × 180.

TABLE I

Uterine pathology associated with the Lippes loop

Pathological diagnoses	Biopsies 21 patients	Hysterectomy specimens 8 patients
Proliferative endometrium		
1. Chronic endometritis	1	3
a. with myometritis	Biopsy only	(2)
b. with adenomyosis	Biopsy only	(2)
2. Stromal lymphocytosis	8	2
3. Subepithelial leukocytes	2	0
4. No abnormality	3	1
Progestational endometrium		
1. No abnormality	6	2
Menstrual endometrium		
1. No abnormality	3	0

logical occurrence at specific stages of the menstrual cycle. Traditionally, it has been necessary to find certain histological criteria, such as the presence of plasma cells, in order to make the diagnosis of bacterial infectious endometritis[9]. These criteria have been established in order to differentiate pathological bacterial endometritis from the normal physiological inflammatory cell infiltration. Reliance on these strict criteria may account for the relatively uncom-

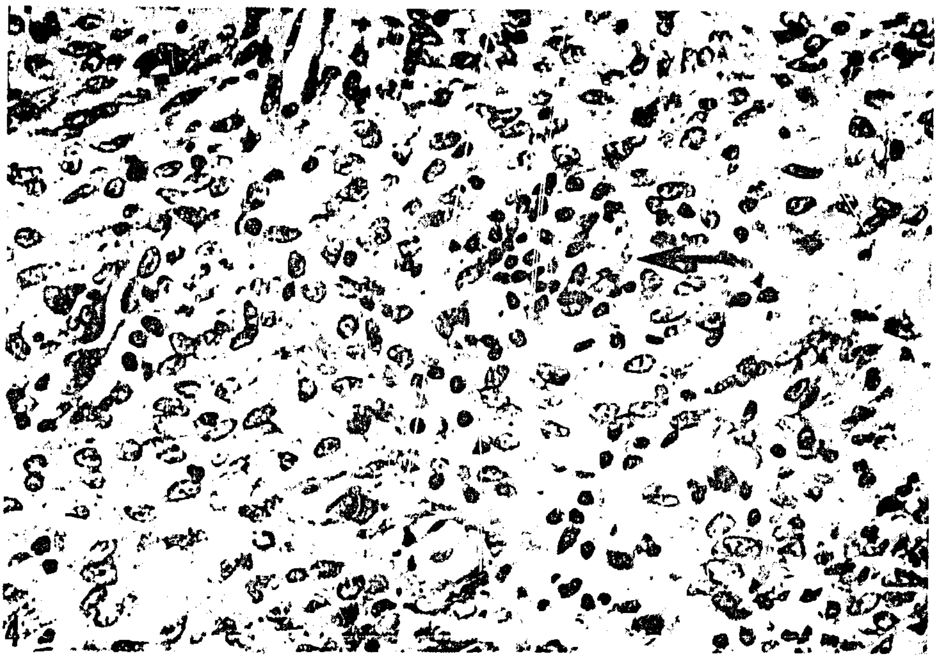

Fig. 4. Lymphocytes (<—) in endometrial stroma. Magnification ×440.

mon reports of endometritis associated with the intra-uterine device. Various investigators have noted that the arrival and disappearance of the inflammatory cells in the endometrium occur at precise times in the cycle[1,9,14]. It seems reasonable that a pathological condition exists, and may be described, whenever the type or quantity of inflammatory cells or reaction is different from the normal physiological, histological pattern described by these investigators.

Thus, even though at the present time the exact significance of the morphologic changes described above is not known, they represent a pathological condition. An attempt has been made to classify these changes into specific descriptive categories. Stromal lymphocytosis with or without lymphoid follicles may be found in patients with tuberculosis, prolapse of pelvic organs, carcinoma of the cervix, pelvic inflammatory disease, and cystic hyperplasia.[2,12] Subepithelial accumulations of leukocytes have been described in patients without intra-uterine foreign bodies and the etiology is obscure.[3] The involvement of the lymphatics in the myometrium of the hysterectomy specimens may account for the development of parametritis in some of these patients.

It appears that definite pathological changes occur in the endometrium of a relatively high percentage of patients having an intra-uterine device. Even though these changes are not significant enough to be classified as endometritis, they are abnormal and should be noted and classified. Further work needs to be done to determine whether the abnormal accumulations of inflammatory cells are associated with a bacterial infection or whether they represent a sterile irritation of the endometrial mucosa as suggested by Lippes.[6]

Summary

Tissue reactions in endometrium and myometrium occur in response to a foreign body even though the devices are made from relatively inert plastics. The response ranges from a mild

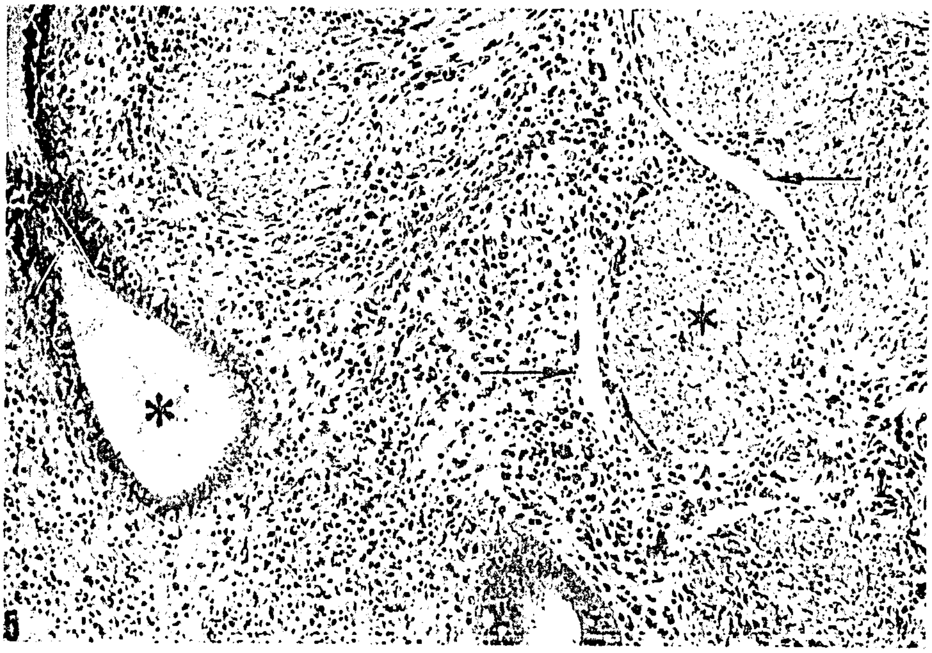

Fig. 5. Lymphocytes and plasma cells infiltrating stroma of uterine adenomyosis contiguous with two lymphatics (←). Note endometrial gland (✱) in focus of adenomyosis and myometrium (★). Magnification ×90.

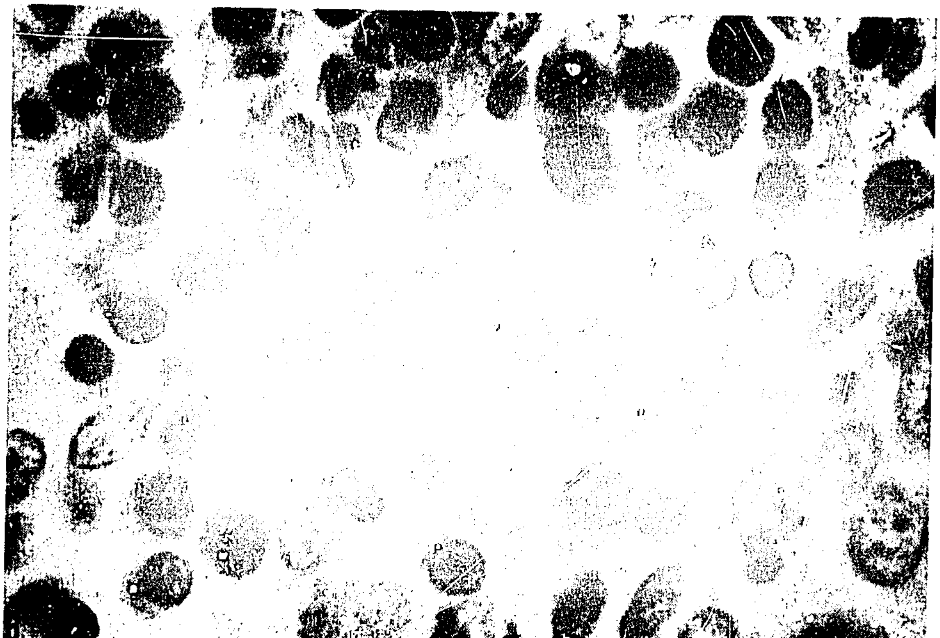

Fig. 6. Plasma cells and lymphocytes in focus of adenomyosis (Figure 5). Magnification ×970.

subepithelial leukocytic infiltration to a diffuse chronic inflammation involving the endometrium and myometrium and their vessels. Only rarely was clinical symptomatology associated with the histologic changes. The significance of these cellular infiltrations is at present unknown.

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STUDIES OF THE ENDOMETRIUM IN PATIENTS USING INTRA-UTERINE CONTRACEPTIVE DEVICES.

II: EVALUATION OF BACTERIOLOGIC METHODS IN CULTURING ENDOMETRIAL TISSUE

by

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Introduction

It has been shown in Part I of this study that there are histological changes in the endometrium associated with the intra-uterine device, which, although abnormal, cannot always be classified as endometritis. These tissue responses range from a mild subepithelial infiltration of leukocytes to a diffuse inflammatory exudate complete with lymphocytes and plasma cells involving the myometrium as well as the endometrium. These histologic findings raise a major question: Is the cavity of the nonpregnant uterus commonly contaminated by bacteria as suggested by Bollinger[1], or does the presence of lymphocytes and leukocytes represent a sterile reaction to the foreign body itself, as suggested by Lippes[5]? In an effort to answer this question, a study to investigate the bacteriologic status in the endometrial tissues was begun.

It was apparent early in the course of the study that certain difficulties would be encountered. In order to culture the human endometrium *in vivo*, it is necessary to traverse the endocervical canal. For practical purposes, the endocervix is usually contaminated with bacteria[1, 6]. Thus, the possibility of the culture device becoming contaminated by its passage through the bacteria-filled canal or by its pushing bacteria-laden mucus into the endometrium was immediately apparent. In an attempt to circumvent this problem, two techniques were utilized, each in a different group of patients. The preliminary results of this study are presented here in order to help define the problems involved in a study of this type and to delineate the rigid criteria which must be observed before the question of bacterial infection of the endometrium can be answered.

Materials and methods

Three groups of patients were studied. In the first group of 24 postpartum patients, endometrial cultures and biopsies were taken between 6 and 8 weeks following delivery. The cervix was prepared by withdrawing as much mucus as possible and then cleansing the cervical os and ectocervix with a 1:750 benzalkonium solution and wiping the cervix dry with sterile cotton applicators. A sterile Rock-Garcia curette, covered by a sterile finger cot, was introduced into the uterine cavity. The finger cot was punctured by withdrawal after the leading tip of the curette had just passed the internal os. The curette was further inserted and a segment of endometrial tissue was taken for culture, and the curette reinserted for a tissue biopsy. The tissue for culture was placed in thioglycollate medium and later subcultured into appropriate media. All bacteria grown were identified and recorded.

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The second group was made up of 27 patients, 6 to 12 weeks postpartum, who desired to use the intra-uterine device for birth control. Prior to insertion of the intra-uterine device a culture of cervical mucus was obtained with a sterile swab and immediately placed in thioglycollate broth. The endocervix was cleansed and dried as above, and an endometrial culture and biopsy obtained with a sterile Rock-Garcia curette. The finger cot technique described above was not used.

The third group of patients were those scheduled to have elective vaginal hysterectomies in association with colporrhaphy for symptomatic uterine and vaginal relaxation. All these patients were from three to six months postpartum. Eight of these patients had the intra-uterine device inserted at some time prior to the surgery. (See Part I of this study.) Ten patients did not have the device inserted and were used as controls. All patients were of the same general age and parity. Immediately after removal of the uterus, it was taken to the bacteriology department by one of us (J.B.), and the anterior surface of the fundus was sterilized by searing with a red-hot metallic spatula blade. A sterile incision was then made into the endometrial cavity, and a portion of endometrium was removed with a sterile bone curette. Portions of the specimen were then placed in five types of culture media: serum broth, thioglycollate broth, cooked meat broth, blood agar plate (aerobic), and chocolate agar plate (anaerobic). Histologic sections of anterior and posterior strips of endometrium were taken from the fundus through the cervix.

Results

In the first group of 24 postpartum women, endometrial cultures followed by an endometrial biopsy were performed, and no cervical cultures were taken. All biopsies showed varying degrees of inflammatory cell infiltration, and the results are seen in Table I. Four of the biopsies showed evidence of inflammatory cells including plasma cells within the stroma, and all were accompanied by positive cultures. The remaining 20 biopsies showed varying numbers of diffuse lymphocytes throughout the stroma with an occasional biopsy showing lymphoid follicles. Half of these patients had positive cultures and the other half negative cultures. There was no clear correlation between the numbers of lymphocytes and the positive or negative cultures.

TABLE I

Endometrial cultures correlated with histomorphological changes in 24 postpartum women

Diagnosis	Positive cultures	Negative cultures
Stromal lymphocytosis	10	10
Chronic endometritis	4	0

Because of the inconclusive correlation of culture and biopsy data in the above group of patients, it was decided that a culture of cervical mucus taken prior to the endometrial culture and biopsy would act as a control on the method in an attempt to rule out contamination by cervical mucus. The second group of 27 patients underwent bacteriological culture of the cervix, in addition to the endometrial culture and endometrial biopsy. As seen in Table II, 12 patients had a positive cervical and a negative endometrial culture. Eight patients had a positive cervical and endometrial culture, each having the same organism(s). Two patients had positive cervical and positive endometrial cultures; however, the cervical organisms were different from the organisms recovered from the endometrium. Five patients had negative cervical and negative endometrial cultures. No patient had a negative cervical and a positive endometrial culture.

TABLE II

Endometrial and cervical mucus cultures correlated with endometrial morphology in 27 postpartum women

Patients	Cultures	Stromal lymphocytosis	Chronic endometritis
12	Positive cervical Negative endometrial	8	0
8	Positive cervical Positive endometrial (same organism)	5	1
2	Positive cervical Positive endometrial (different organism)	1	1
5	Negative cervical Negative endometrial	4	0

Histological correlation with the above four culture groups is as follows: Eight of the 12 patients with positive cervical and negative endometrial cultures showed evidence of varying numbers of diffusely scattered lymphocytes throughout the stroma. Five of the eight patients who grew the same organism from cervical and endometrial cultures showed stromal lymphocytosis, and one showed evidence of histological chronic endometritis. Of the two patients with positive cervical and endometrial cultures but with different organisms, one showed histological evidence of chronic endometritis and the other stromal lymphocytosis. Four of the five patients with negative cervical and endometrial cultures showed histological evidence of stromal lymphocytosis. Further questioning of the patients in this last group revealed that a vaginal douche was done prior to the clinic visit, and it is possible that anti-bactericidal components were present in the douche material.

Tables III and IV show the spectrum of bacteria recovered from the cervical mucus and

TABLE III

Spectrum of bacteria recovered from cervical mucus in 36 postpartum patients

Aerobacter aerogenes	6
Escherichia coli	1
Escherichia intermedius	3
Proteus vulgaris	1
Staphylococcus albus	7
Staphylococcus aureus, coagulase negative	3
Streptococcus, anaerobic	2
Streptococcus fecalis	2
Streptoccoccus mitis	11
Streptococcus sanguis	5
Streptococcus zymogenes	3

endometrium, respectively, of the postpartum patients. These organisms are similar to the normal flora of the vagina and cervical mucus found by other investigators.[1,6]

TABLE IV

Spectrum of bacteria recovered from endometrium in 24 postpartum patients

Aerobacter aerogenes	7
Escherichia coli	2
Escherichia intermedius	5
Staphylococcus albus	2
Streptococcus, anaerobic	1
Streptococcus fecalis	1
Streptococcus mitis	4
Streptococcus sanguis	3
Streptococcus zymogenes	3

In an effort to eliminate the possibility of pushing cervical mucus into the endometrial cavity prior to culture, transfundal cultures on hysterectomy specimens were performed. Of all ten postpartum patients who had no intra-uterine device, all cultures were negative from the endometrium and cervix with the exception of one cervical culture (Table V). Eight postpartum patients, in whom the Lippes loop was inserted from two to thirty days prior to operation, had negative endometrial and cervical cultures with the exception of one positive cervical culture. In view of the large number of negative cervical cultures, investigation was made of the procedures associated with the operation. Investigation of the pre-operative work-up revealed that a Furacin suppository was inserted in all patients into the vagina on the evening prior to surgery, and that the entire vaginal area was further disinfected by a hexachlorophene scrub just prior to the operation. It was felt that these antibacterial procedures produced the large incidence of negative cervical (and possibly endometrial) cultures in the hysterectomy patients. Further studies are now being undertaken in a group of patients without preoperative antibiotics to determine the bacteriological flora, utilizing the transfundal technique of endometrial culture.

TABLE V

Endometrial and cervical mucus cultures of hysterectomy specimens in 8 IUCD and 10 control postpartum patients

	Cultures			
	Cervical		Endometrial	
Patients	Negative	Positive	Negative	Positive
IUCD	7	1	8	0
Control	9	1	10	0

Discussion

Certain fundamental principles of interpretation of results were learned from this preliminary study. In the first group of patients, false positive endometrial cultures apparently occurred as a result of contamination with cervical mucus. Although a large percentage of the endometrial cultures grew bacteria, there was no correlation between the number of inflammatory cells seen histologically and either the positive or negative cultures. Several endometrial cultures were positive in which only very rare inflammatory cells were found in the biopsy.

In this first group of patients, attempts were made to take the endometrial culture by placing a sterile finger cot over the curette, and puncturing the cot after passing the internal os. This method, in addition to being cumbersome, could not always be considered reliable, as the finger cot itself might carry bacteria from the endocervix to the endometrium. It was then decided, in the second group, to take cervical cultures in order to establish controls on each specimen. Since several biopsies taken with the loops in place had shown that the inflammatory exudate was located only deep in the stroma surrounding the glands, it was decided that endometrial tissue should be used for the culture material. Endometrial washes might give false negative results.

In the third, or hysterectomy, group of patients, there was little concern about obtaining false positive endometrial cultures since the transfundal method was utilized in obtaining them. Instead, false negative cultures might occur if the patient had been prepared for surgery with a bactericidal vaginal suppository or douche. This finding became apparent early in the study, and the routine preoperative vaginal preparation was discontinued. Undue delay between extirpation of the uterus and culturing of the endometrial cavity might also give false negative results. Therefore, the uteri were taken from the operating room to the bacteriology department immediately after their extirpation. It was necessary to take cervical cultures in these specimens also in order to establish controls.

Although various methods of obtaining "sterile" endometrial cultures have been proposed[1,2,3,4] the problem of avoiding contamination by cervical mucus is always present. It is necessary to establish rigid criteria in order to accurately assess the results obtained in both groups of patients. These criteria may be listed as follows: Presumptive evidence of endometrial infection exists only when (1) the endometrial culture contains an organism which is different from the organisms of the endocervix, and (2) there is histologic evidence of inflammation. Presumptive evidence of a lack of endometrial infections exists only when (1) the cervical mucus has a positive bacterial culture and culture of the endometrium is negative, and (2) there is no histologic evidence of infection. Equivocal evidence of endometrial infection exists, using the transcervical culture method, when the endometrium and cervical mucus contain the same organisms. When this situation exists, it is uncertain whether there is contamination from the endocervical canal into the endometrium or whether contaminated endometrial fluid drains down into the endocervical canal. Since the cervical mucus is infected in most patients, there is evidence of induced bacteriologic sterility, either from the patient taking antibiotics or using a douche, when there is a negative cervical culture and the endometrial culture is either positive or negative.

A continuing study is being done using these methods and these criteria of evaluating the methods to determine whether or not the histological inflammatory action evoked by the intra-uterine device is caused by a bacterial infection.

Summary

Methods of culturing endometrium were determined in three groups of patients. The transcervical method produced a high number of false positive endometrial cultures when correlated with the biopsy. By using cervical mucus cultures as a control, more accurate evaluation of endometrial culture results were obtained. A transfundal method of obtaining sterile endometrium from hysterectomy specimens has been described.

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UTERINE HISTOPATHOLOGY IN THE PRESENCE OF INTRA-UTERINE DEVICES

by

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Introduction

Various laboratory and clinical approaches have been undertaken to investigate the effectiveness, safety, and mode of action of intra-uterine contraceptive devices. It has already been shown that sperm migration is not affected in the presence of a device, and tubal pregnancies have also been reported. The purpose of the present study is to investigate the effect of intra-uterine devices and to evaluate endometrial response to ovarian hormones in the presence of a foreign body.

Materials and method

One hundred women of proven fertility attending the Family Planning Clinic at the All-India Institute of Medical Sciences, Delhi, were selected for the study. All had regular menstrual periods and wanted intra-uterine devices for contraception. Endometrial biopsies were taken just prior to insertion to serve as controls. Strips of endometrium were obtained from both the anterior and posterior walls of the uterus. Biopsies were then repeated after intervals of 1, 3, 6, 9, 12, 18, and 24 months. Samples were taken in the proliferative as well as the secretory phase of the menstrual cycle with the device in place. Biopsy material was subjected to histological examination and endometrium was dated according to the criteria of Noyes *et al.*[2] Endometrial biopsies were also repeated in some patients with a history of heavy or irregular bleeding.

Intra-uterine devices were also inserted in nine women scheduled for elective vaginal hysterectomy. Insertions were done one to four months prior to surgery. After removal the uteri were subjected to histological examination, and areas free from the device as well as those in firm contact with the device were sectioned.

Observations

Dating of all control endometrial biopsies corresponded with the day of the menstrual cycle on which the biopsy had been taken. Of the repeat biopsies, 41 were taken in the proliferative phase and 46 in the secretory phase of the menstrual cycle. The remaining 13 biopsies were taken from women who had complaints of heavy, moderate, irregular, or continuous bleeding since the insertion of the device. In the heavy or continuous bleeders, the biopsy was taken just prior to the removal of the device.

Histological examination revealed proliferative type of endometrium in 48 biopsies (as shown in Figure 1), which included four women with lactational amenorrhea. There was no

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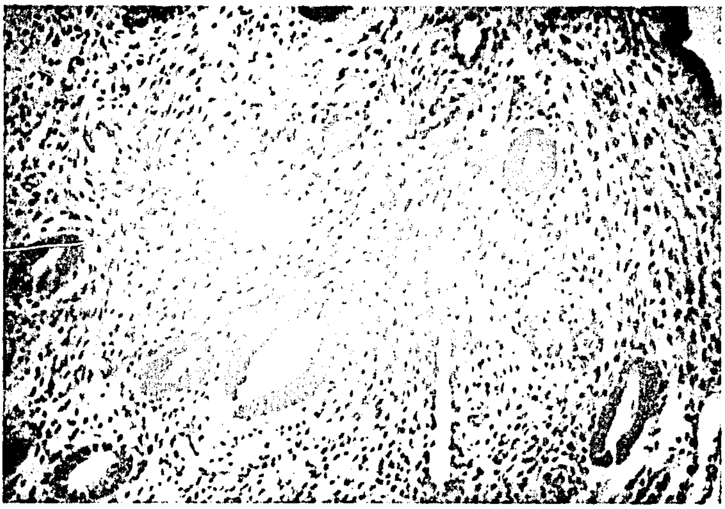

Fig. 1. Endometrial biopsy taken in the proliferative phase, with the intra-uterine device in place.

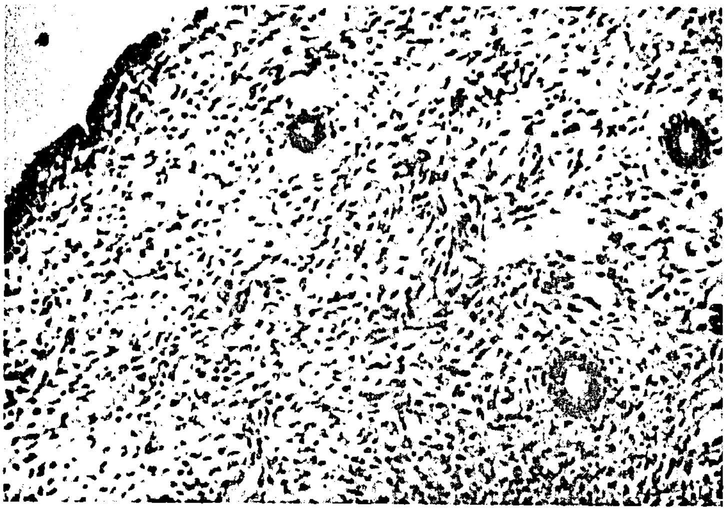

Fig. 2. Biopsy taken from a patient with lactational amenorrhea two months after insertion of the intra-uterine device. Proliferative glands are seen.

evidence of endometritis, as judged by the presence of plasma cells and over 5 polymorphs per HPF. Included in this group are 7 biopsies taken from women with a history of bleeding. Three women had continuous heavy bleeding for 2 to 3 months and the device had to be removed. The remaining 4 women had moderate bleeding at irregular intervals; none of the bouts of bleeding could be classified as menstrual periods.

Secretory endometrium was seen in 46 specimens as shown in Figures 2 to 7. Dating of the endometrium corresponded with the day on which the biopsy had been taken, indicating

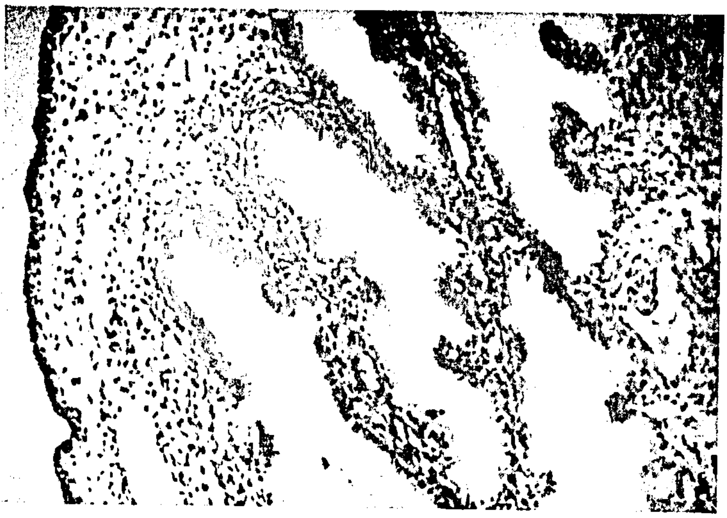

Fig. 3. Endometrial biopsy, showing secretory endometrium, taken on day 22 of menstrual cycle with the intra-uterine device in place.

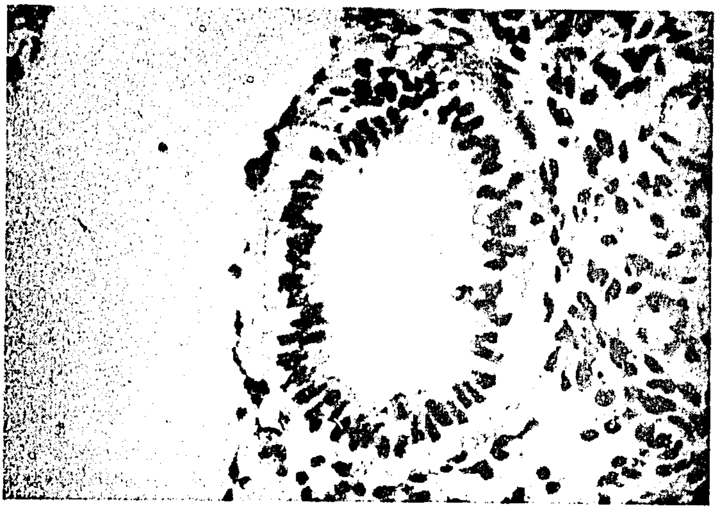

Fig. 4. Endometrial biopsy taken on day 16 of the menstrual cycle, one month after insertion of the intra-uterine device. Basal vacuoles in the glands are prominent.

ovulation and normal response of the endometrium to ovarian hormones. No inflammatory or foreign body reaction was noted. Similar observations were made on samples taken at 1, 3, 12, 18, and 24 months' intervals.

Sections from uteri obtained by vaginal hysterectomy revealed no changes in the development of the endometrium and no foreign body or inflammatory reaction.

A mixed type of endometrial response was seen in six biopsies. Both proliferative and

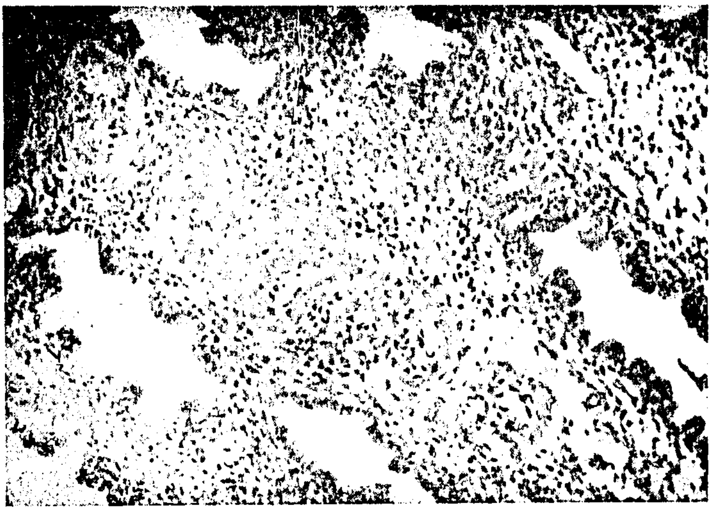

Fig. 5. Biopsy taken on day 24 of menstrual cycle, nine months after insertion of the intra-uterine device. Note strong pre-decidual reaction around the arterioles and secretory type of glands. No foreign body type of reaction noted.

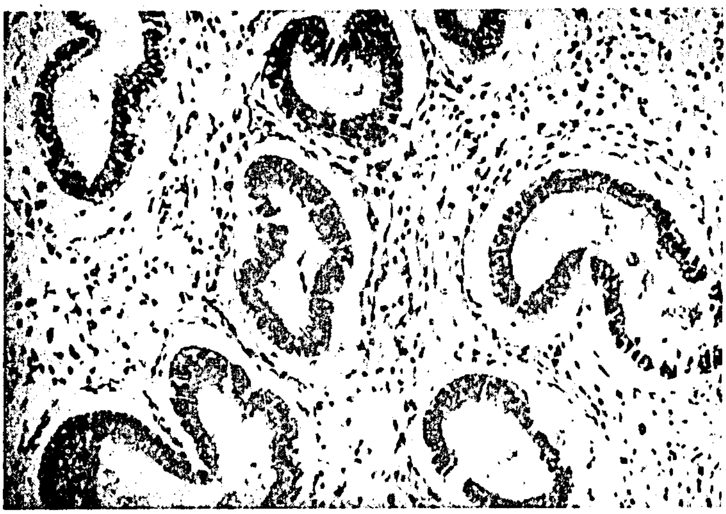

Fig. 6. Endometrial biopsy taken on day 21 of the menstrual cycle, twelve months after insertion of the intra-uterine device. Secretory type of endometrial glands with stromal edema are seen. No evidence of inflammatory reaction noted.

Secretory types of endometrium were seen in different fields of the same section as shown in Figures 8 and 9. Of the six patients, three had heavy bleeding, warranting removal of the device in two cases. The remaining three had moderate to mild bleeding off and on, without any regular menstrual periods.

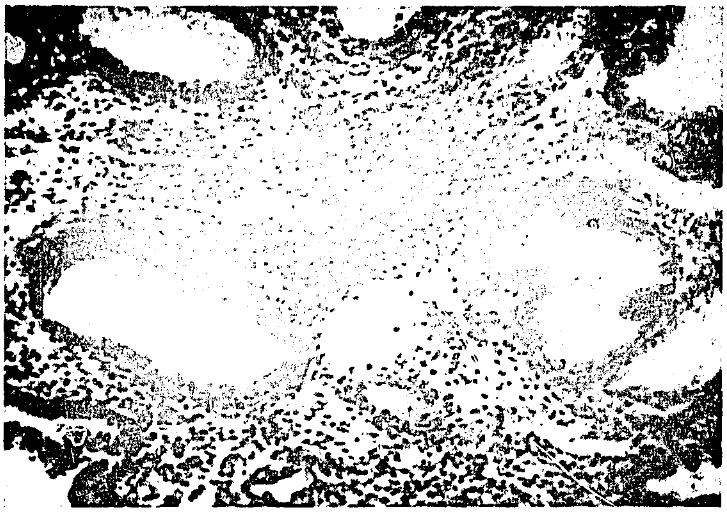

Fig. 7. Biopsy taken on day 23 of menstrual cycle, eighteen months after insertion of the intra-uterine device. Secretory glands and stromal edema seen.

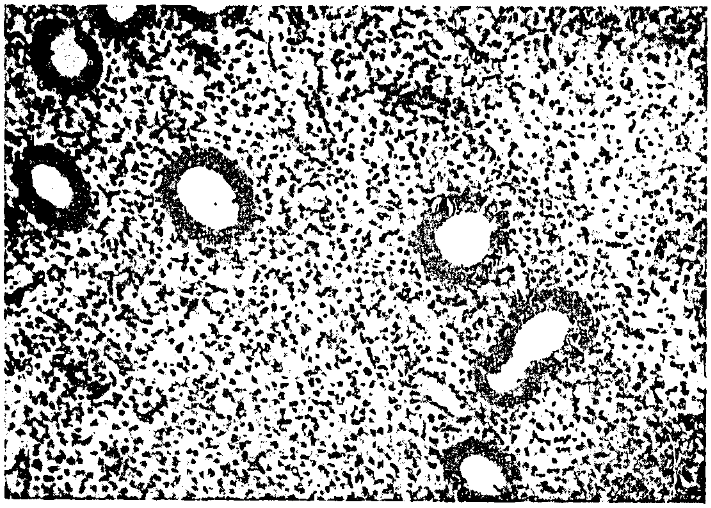

Fig. 8. Endometrial biopsy taken from a patient bleeding for fifteen days after insertion of the intra-uterine device. Note proliferative type of endometrial glands.

Comments

From the present study it appears that the intra-uterine contraceptive device does not affect ovulation and that the cyclic changes of the endometrium, secondary to ovarian hormones, remain unaltered. The degree of progestational change was similar to that of controls and no foreign body reaction, endometritis, or vascular changes were noted in the biopsy or hysterectomy samples. Although the exact mode of action of intra-uterine devices is not known,

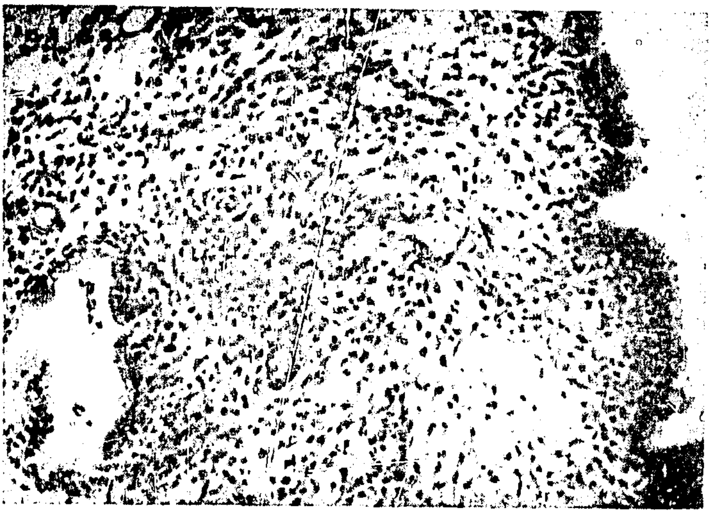

Fig. 9. Another area from the same section in the same patient as in Figure 8. Note stromal edema, secretory glands, and some pre-decidual reaction around arterioles.

it is probably other than inhibition of ovulation, or alteration in the response of the endometrium to ovarian hormones.

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GENITAL TRACT INFECTION WITH AN INTRA-UTERINE CONTRACEPTIVE DEVICE: A HISTOPATHOLOGIC STUDY

by

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The most important of the complications which resulted from the use of stem pessaries were soft-tissue damage and serious pelvic infections. In an attempt to circumvent these problems, without losing the advantage of a permanently placed contraceptive device, Gräfenberg devised his intra-uterine ring. Unfortunately the metal spirals, although a distinct improvement over stem pessaries, also caused tissue damage, occasionally even eroding into the myometrium. This provided a source of entry for pathogenic bacteria and consequent infection of the genital organs, occasionally serious enough to cause permanent sterility and even death. Because of these undesirable side effects most gynecologists stopped using Gräfenberg rings and most teachers condemned them. It is not surprising therefore that present-day physicians have reservations concerning the safety of the new intra-uterine devices despite their many obvious advantages over other contraceptive methods. The main concern is that a foreign body in the uterus—even one made of inert polyethylene—may cause tissue damage, be a source of infection, or even predispose to the development of cancer.

Gynecologists who have continued to use the intra-uterine contraceptives state that the incidence of pelvic infection is low, even for those which remain in place many years.[2,4] The truth of this statement is borne out by the fact that few develop symptoms suggestive of infection. In addition fertility is unimpaired; many women conceive within a month or two after a device they have worn for a long period of time is removed. In our study of the bacterial flora of the endometrial cavity neither the incidence of positive cultures nor the distribution of bacteria was altered in 200 women who were wearing *Permaspirals*.[6]

Six hundred and twenty-three women who were attending the gynecologic clinic of the Temple University Medical Center, Philadelphia, wore *Permaspirals* for a total of 5,606 months. Forty-eight (7.7%) developed pelvic infections, of which 43 involved the upper genital tract and 5 the cervix alone. Gonococci were identified as the responsible organisms in 10. Although the number of infections appears high they cannot be attributed solely to the presence of the device because an infection rate of this magnitude is not unusual for the women included in this study. Jessen had a similar experience with a comparable group of indigent patients.[3] Quite in contrast we know of no infection which has developed in a private patient in whom we have inserted an intra-uterine pessary.

Since it is essential to know what effect an intra-uterine device has on uterine tissues this study was devised to determine whether or not .ne incidence of endometritis is increased in women who are wearing *Permaspirals*.

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Materials and method

The 171 women included in the study were indigent or semi-indigent ward patients who were attending the Gynecologic Clinic of the Temple University Medical Center. All had had at least one child, the most recent one having been born in the Temple University Hospital. Of the 144 women who were studied both before and after the insertion of an intra-uterine contraceptive device, 103 (71.5%) had been delivered less than four months before the first examination. Several had been treated for acute pelvic inflammatory disease prior to the most recent delivery, but none had any obvious pelvic abnormality when she was admitted to the study.

Material was obtained from the cervical canal and from the endometrial cavity for bacterial cultures, after which an endometrial biopsy was performed. A *Permaspiral* was then introduced into the uterine cavity. The spiral, the introducer, and the instruments used to obtain the material for culture and biopsy were all sterile. Excess vaginal and cervical secretions were removed with dry sterile cotton balls, but no attempt was made to sterilize the vagina or the cervix.

Endometrial biopsies were obtained from 144 women immediately before the spirals were introduced and at least once more while the devices were in place. Biopsies were obtained also from 27 women who were wearing spirals and in whom unusual amounts of bleeding, pain, or discharge had developed; none of these had had pre-insertion studies. A total of 203 postinsertion biopsies were taken from the 171 women. The maximum time a spiral had been in place was 24 months.

Diagnostic criteria

After consulting numerous textbooks and published articles and talking with several pathologists we found that criteria for the classification of the various types of endometritis are not clearly defined. There is no problem when endometrial infection occurs in conjunction with acute salpingo-oophoritis or induced abortion; under these circumstances all the layers of the endometrium are diffusely infiltrated with polymorphonuclear leukocytes, there is loss of the superficial epithelial layers and spindling of the stromal cells; bacteria can usually be identified in the tissue or in the secretions.

Chronic endometrial infection presents quite a different picture. Polymorphonuclear leukocytes may be scattered throughout, but lymphocytes and plasma cells predominate and are more characteristic. A chronic infection can be suspected when the numbers of plasma cells and lymphocytes are increased to a point at which they are distributed uniformly throughout the upper layers of the endometrium and can be seen in almost every field. In addition the stroma may be more vascular than usual with an increased number of thick-walled blood vessels in the deeper layers. Spindling of the stromal cells and edema may also occur, but slight changes are hard to evaluate.

The difficulty in accurately interpreting the histologic changes resulting from minor endometrial infections stems from the fact that similar changes can also be detected during the normal menstrual cycle. Lymphocytes, plasma cells and even polymorphonuclear leukocytes can almost always be found in normal endometrium; they usually do not appear in every high-power field and rarely are clumped. In the immediate premenstrual phase and during episodes of bleeding, menstrual as well as abnormal, the stroma may be diffusely infiltrated with polymorphonuclear leukocytes as well as with lymphocytes, presenting a picture much like that of active endometritis. There may be spindling of the stromal cells during the early proliferative phase. Considerable edema, particularly in the middle layers, can usually be seen during the postovulatory phase of the cycle.

Leukocytic infiltration also occurs regularly during uterine involution after delivery. Sharman[5] states that lymphocytes first begin to replace polymorphonuclear leukocytes in the stroma on about the eighth day and that plasma cells appear on about the tenth day. He detected lymphocytic and plasma cell infiltration in 37 percent of 400 endometrial specimens obtained during the third and fourth postpartum months. He does not consider this to be indicative of endometrial infection.

Our criteria for diagnosing endometritis (positive biopsy) are as follows: (1) The appearance of at least 5 polymorphonuclear leukocytes in almost every high-power field with occasional clumps of inflammatory cells. The infection is considered to be acute if the tissue is diffusely infiltrated and polymorphonuclear leukocytes predominate. (2) The recognition of at least 5 lymphocytes or plasma cells in almost every high-power field. These are more characteristic of chronic infection.

Endometritis was not diagnosed if there was a considerable amount of stromal hemorrhage even though there was adjacent leukocytic infiltration. A slide was considered positive, however, if the diffusion of blood was slight and if the predominant cells were plasma cells and lymphocytes. Minor variations in stromal cell spindling and in edema occurring in conjunction with an inflammatory process often are difficult to evaluate in endometrial biopsy specimens; consequently, our diagnoses were based primarily on cellular infiltration.

Results

Pre-insertion biopsies. Endometrial tissue which was adequate for evaluation was obtained from 144 women immediately before the spiral was inserted. In 20 (13.8%) the infiltration of plasma cells and leukocytes was considered to be greater than normal; these were diagnosed as positive; 124 (86.2%) were considered to be normal.

Relationship of biopsies to delivery. The interval between delivery and the biopsy is known in 140 women. Of the 103 who had delivered less than 4 months previously the biopsy was positive in 18 (17.5%) and normal in 85 (82.5%). In only 2 of the 37 women who were more than 4 months postpartum was there abnormal cellular infiltration in the biopsy material (Table I).

TABLE I

Pre-insertion endometrial biopsies

Months after delivery	<2	<3	<4	<5	<6	6–12	>12	Unknown
Positive	9	7	2	0	0	1	1	
Normal	31	40	14	13	5	11	6	4

In 4 of the 20 positive biopsies the cells were predominately polymorphonuclear leukocytes which were scattered throughout the stroma, but the tissue was not diffusely infiltrated. These were classified as mild acute endometritis. Three of these women had been delivered less than 2 months previously and the fourth was less than 4 months postpartum.

Postinsertion biopsies. Endometrial tissue which was adequate for evaluation was obtained 184 times while the spiral was in place. In 36 (19.6%) the infiltration of round cells was considered to be greater than normal; these were classified as positive; 148 (80.4%) were considered to be normal.

Thirty-four of the positive biopsies were classified as chronic endometritis on the basis of a diffuse sprinkling of plasma cells, lymphocytes, and only occasional polymorphonuclear leukocytes. In none was there any great concentration of cells either diffusely distributed or clumped. Acute endometritis was diagnosed in the other 2 patients. In one with an acute exacerbation of chronic salpingo-oophoritis, the endometrial stroma was diffusely infiltrated with polymorphonuclear leukocytes. In the other the polymorphonuclear infiltration was much less, but cells of this type were evident in almost every field.

Relationship to number of months the spiral was used. Positive biopsies were obtained in 50 percent of 22 women during the first 3 months the spiral was in place. In those who had worn devices between 3 and 6 months the incidence of positive biopsies was 12.9 percent; between 6 and 12 months, 14.6 percent; and between 12 and 24 months, 28 percent (Table II).

TABLE II

Postinsertion endometrial biopsies

Months with spiral in place	<3	3–6	6–12	12–24	Unknown
Positive	11	7	11	7	
Normal	11	48	64	18	7

The increased incidence of positive biopsies during the first 3 months of use is probably related to the fact that so many of the women had been delivered 2 or 3 months previously and to bleeding which occurs so frequently during the first few cycles after the spiral is inserted. This obviously is a transient phenomenon since it did not persist.

Relationship of biopsies to endometrial cultures. The relationship between leukocytic infiltration in the endometrium and endometrial bacterial cultures is shown in Table III. The incidence of positive cultures at the time of insertion is almost identical in those with positive pre-insertion endometrial biopsies (58 percent) and in those considered to be normal (60.5 percent).

The incidence of positive cultures with the spiral in place is higher in those with positive

TABLE III

Relationship of biopsies to cultures

Pre-insertion		Post-insertion	
Biopsy	Culture	Biopsy	Culture
Positive — 20	Positive — 11 No growth — 8 No culture — 1	Positive — 36	Positive — 15 No growth — 11 No culture — 10
Normal — 124	Positive — 69 No growth — 45 No culture — 0	Normal — 148	Positive — 56 No growth — 57 No culture — 35
Inadequate — 10		Inadequate—19	

postinsertion endometrial biopsies (57.7 percent) than in those considered to be normal (49.6 percent).

Relationship of biopsies to symptoms. Most biopsies were obtained whenever the patients returned for follow-up examinations regardless of the stage of the cycle or the presence of symptoms. However, 27 returned for examination specifically because of symptoms and the biopsies were obtained as an aid in evaluating the complaint. Twenty-one had intermenstrual spotting and one was menstruating heavily, three complained of abdomino-pelvic pain and two had an acute pelvic infection. Fourteen of these biopsies were diagnosed as positive (Table IV).

TABLE IV

Relationship of biopsies to symptoms

Pre-insertion	
Asymptomatic — 140	Positive biopsy — 19 Normal biopsy — 121
Symptomatic — 4 Intermenstrual bleeding — 1 Menses — 3	Positive biopsy — 1 Normal biopsy — 3
Postinsertion	
Asymptomatic — 157	→ Positive biopsy — 22 → Normal biopsy — 135
Symptomatic — 27 Intermenstrual spotting — 21 Pain — 3 Menses — 1 Clinical PID — 2	→ Positive biopsy — 14 PID — 1 Intermenstrual spotting — 13 → Normal biopsy — 13 PID — 1 Pain — 3 Intermenstrual spotting — 8 Menses — 1

Discussion

The criteria for the diagnosis of endometrial infection, with the exception of acute endometritis, are not well established. One of the common errors in the interpretation of endometrial histology is to diagnose endometritis on the basis of leukocytic infiltration of the stroma during the premenstrual phase of the cycle. Curtis[1] was one of the first to recognize this as a physiologic reaction. In an important study of endometrial changes in normal women and those with pelvic infections he commented upon the frequency with which he had observed polymorphonuclear leukocytic infiltration without evidence of infection during episodes of bleeding. In addition, he observed that while plasma cells appear regularly in response to inflammation they are not necessarily indicative of an active infection. He could not regularly identify bacteria in endometrial specimens which were diffusely infiltrated with plasma cells. He also stated that plasma cells often are found in association with edema in endometria in which there is no other evidence of an inflammatory response.

Most pathologists agree that scattered leukocytes of all types can be identified in the superficial layers of the endometrium throughout the entire cycle and that this in itself does not denote infection. In normal tissues lymphocytes and plasma cells predominate, they are sprinkled irregularly throughout the section, and they do not appear in every high-power field. Localized collections of round cells are not often seen.

The presence of the Margulies *Permaspiral* apparently did increase the incidence of histologic endometritis; 13.8 percent of pre-insertion biopsies were positive as compared to 19.6 percent during the months it was in place. The difference is even greater when we consider that most of the pre-insertion biopsies were taken during the first four postpartum months, when a high incidence of leukocytic infiltration can be anticipated.

It is important to note, however, that the ratio of normal to positive biopsies was about the same before the device was inserted and while it was in place in women who had neither intermenstrual bleeding nor abnormal symptoms. The increase in positive postinsertion biopsies resulted primarily from our investigation of 27 women who were studied only after insertion of the spiral and specifically because of the appearance of a symptom.

The presence of the device did not alter the incidence of positive bacterial cultures in those with positive tissue biopsies. Bacteria were identified in 58 percent while the spiral was in place. Comparable figures for those with negative tissue biopsies were 60.5 percent positive cultures before insertion and 49.6 percent after. It is difficult to draw precise conclusions from these figures but they suggest that there may be a relationship between the presence of the spiral, the positive tissue biopsy, and the positive bacterial culture. In a previous study we obtained positive endometrial cultures in 69 percent of patients two months after delivery, 57 percent during the third month, 61 percent during the fourth month, 50 percent during the fifth month and 55 percent between six and 12 months.[6] The incidence of positive pre-insertion bacterial cultures was almost the same in those with positive and those with negative biopsies: 58 percent and 60.5 percent respectively. This is similar to the general incidence of positive bacterial cultures during the first four postpartum months and is probably a result of the recent delivery. There was a difference in postinsertion culture rates: 57.7 percent for those with positive biopsies and 49.6 percent for those whose tissues were more normal. Although this difference is slight it suggests the possibility that the device may either prolong the interval of postpartum leukocyte infiltration or actually be a responsible factor in the production of endometrial infection.

Many women experience irregular intermenstrual bleeding and increased menstrual flow during the first few cycles after the insertion of an intra-uterine device. In some this may persist for many months. We have assumed that the leukocytic infiltration in the endometria of the women who were bleeding at the time the specimen was obtained was related to tissue disruption, but we cannot completely exclude the possibility that in some the bleeding might have been the result of local infection. That this is not likely is suggested by the fact that the leukocytes were not distributed uniformly thoughout the tissue but predominated in the areas into which the blood had diffused. In addition there were no other consistent histologic evidences of endometritis such as spindling of the stromal cells or ulceration of the epithelial surface.

The histologic changes which are so often present in the endometria of women wearing *Permaspirals* may, at least in part, contribute to the leukocytic infiltration we have diagnosed as endometritis. Submucosal edema, localized hemorrhage and an associated increase in vascular channels in the superficial layers occur frequently and in some sections is quite pronounced. Whether these changes represent a tissue response to infection or whether they are the result of pressure from the spiral has not yet been determined, but is seems likely that the latter is true. In most instances, even those with extensive increases in edema and tissue vascularity, round cell infiltration is inconsequential. One would expect much more evidence of active infection had the edema and vascularization developed in response to bacterial invasion.

Even though we may assume that a mild endometritis does develop there is no evidence to suggest that it becomes progressively more severe during the time the spiral is in the uterus or that there are any serious consequences. The changes we have observed are mild and affect the superficial layers predominately. The endometrium probably returns to a reasonably normal state after each menstrual period. The most important evidence to indicate that the changes are not only reversible, but that the endometrium returns to normal promptly, is the rapidity with which pregnancy occurs after the device is removed. Seven women who had worn *Permaspirals* continuously from three to 25 months conceived promptly after their removal. Five became pregnant in one month, one in two months, and one in nine months: two who had worn spirals 13 and 25 months conceived within one month.

Summary

Endometrial biopsies were obtained from 144 postpartum women before an intra-uterine contraceptive device was inserted and at intervals while it was in place. Endometritis was diagnosed in 20 (13.8 percent) of the pre-insertion and in 36 (19.6 percent) of the postinsertion specimens. There was no increase in the incidence of positive postinsertion specimens in women who had neither abnormal bleeding nor other pelvic symptoms. Fourteen of 27 biopsies that were obtained because of bleeding, discharge, pain or other complaints were positive.

Most of the positive biopsies revealed minor changes similar to those which occur in chronic endometrial infections. Whether these actually represent infection or are simply due to the pressure of the spiral has not yet been determined. The changes were reversible.

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INTRA-UTERINE FOREIGN BODY STUDIES IN RODENTS

by

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A little over two years ago, at the first conference on intra-uterine contraceptive devices, it became apparent that little was known concerning their mode of action in humans or animals. This offered us an excellent opportunity to develop a study which would correlate our basic laboratory research with a current clinical investigation. Ideally, our laboratory findings would then point out what clinical studies should be undertaken to determine the mode of action in primates. It is the basic research or laboratory investigations that I shall be discussing.

To condense two years' work into a short and coherent presentation, it is necessary to omit many details and statistics. Rather, I shall try to give a survey of our major experiments and the conclusions we have drawn from them. For the sake of continuity I shall discuss them chronologically, since we like to think that each of our experiments was the logical outgrowth of the preceding one.

Our first step was a thorough literature search, which revealed only one paper concerning the mode of action of an intra-uterine foreign body (IUFB). In 1932 Carleton and Phelps[1] reported that an IUFB in the rabbit prevented pregnancy by a mechanical action since implantations occurred twice as often above the IUFB as below. Our first studies were undertaken to confirm or contradict these findings. We placed an IUFB, either a small piece of polyethylene catheter or a length of No. 5 suture, in one horn of 10 rabbits, which were then mated to normal bucks. Of these 10, 8 had the IUFB in place at time of autopsy, which was on day 12 or 13 of pregnancy. Four of these animals had no evidence of implantation in either horn, but the remaining four had bilateral implantations, which in the operated horn were above, below, and even on top of the IUFB. Dr. Peter Eckstein also has observed these random implantations in rabbits bearing an IUFB.[2] In addition he has found that the number of implants is less in the treated horn and that the ova that do implant degenerate prior to term. The difficulties we were encountering in breeding our does, combined with the apparent ineffectiveness of the IUFB in rabbits, led us to begin our studies with another rodent, the rat.

Normal adult females of the Long-Evans strain, chosen at random from our colony, were anesthetized with ether and one uterine horn was exposed via a flank incision. A needle with No. 5-0 braided silk suture was introduced through the anti-mesometrial wall of one uterine horn, passed down the lumen and brought back out 5 to 8 mm below the point of entry. A knot at the upper end anchored the suture in place. The suture was then clipped at the lower end and the uterus manipulated slightly so that the suture was retracted into the uterine lumen where it lay free. The animals were closed, checked for stage of estrous cycle by vaginal smear, and placed with a male. Vaginal smears were recorded each subsequent morning, and the day on which either sperm or a copulation plug was found was designated as day 1 of pregnancy.

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Data on vaginal smears from 115 rats demonstrate that the IUFB does not alter the length of the estrous cycle in operated females. By day 8, well over 90 percent of the females had mated, and the number of animals that did not mate during the course of the experiment or had an excessively long period of diestrus prior to mating was well within the normal control range. In short, neither the insertion nor continuing presence of an IUFB altered the estrous cycle or mating behavior in the rat.

Our principal question was what effect the IUFB would have on pregnancy. We killed our first group of animals on various days after implantation should normally have occurred. Implantation had indeed occurred, but only in the control (unoperated) horns. The horn with the IUFB had no evidence of implantation at any point along its length. Both ovaries had corpora lutea, and the operated horn had the gross appearance of a normal non-pregnant uterus. In a few animals there was definite evidence of infection in the operated horn, and these animals were excluded from the experiment. The treated uterine horn and fallopian tubes were flushed, but no ova were found.

Now that we knew an IUFB would block pregnancy in the rat, we could attempt to study its mode of action. Implantations in the control horns ruled out a systemic action, but several local mechanisms had to be studied. Sperm transport could be abnormal, fertilization might not have occurred, tubal transport could be aberrant, the suture might act as a mechanical trap, or the uterine environment might be hostile.

These possibilities were investigated in our second series of experiments, in which the animals were killed on various pre-implantation days. The entire reproductive tract was removed, corpora lutea were counted, and the uterus and tubes were flushed to recover ova. There was no significant difference in the number of ova recovered from the treated and control sides during the first four days, which showed that sperm transport, fertilization, and tubal transport were normal. On day 5, however, when ova reached the uterus, none could be found in the operated horn. Inspection and dissection of the sutures ruled out the possibility that the ova were attached to them. We wondered if the suture might be sufficiently irritating to cause abnormal uterine motility, which would tend to expel the ova before they could implant. Two subsequent experiments tended to rule this out. We found that sutures in the myometrium only, or which only passed across the lumen, did not prevent implantations. Also sutures removed on day 4, in the morning, one full day before implantion occurs and one half day before the ova enter the uterus, still prevented implantation in 3 of 4 animals. The position of the suture in the uterus and the material used were not critical, since nylon and stainless steel were as effective as silk, but less flexible, and an IUFB in the lower half of the uterus gave the same result as one in the upper segment.

Bilateral sutures resulted in bilateral implantation failure and loss of ova from both horns. Females with these bilateral sutures did tend to have prolonged periods of pseudopregnancy. This last observation was made on a very small group of animals, so it is impossible to determine if the lengthening was statistically significant.

The disappearing ova had us baffled. We could not find them in the vagina, nor could we recover them even if the cervices were ligated on the morning of day 4 and ova recovery attempted late that evening or early the next day. We wondered if some alteration had occurred in the uterine environment that resulted in destruction of the ova, so we began to investigate the effect of the IUFB on the uterus, using the classic method of Loeb to estimate uterine sensitivity – the formation of deciduomata in response to a traumatic stimulus. Animals with bi- or uni-lateral sutures received either 0.5 mg of histamine intraluminally or a second traumatic suture on day 4 or 5 of pregnancy. At autopsy 3 to 4 days after the second operation, none of the uterine horns with an IUFB in place showed deciduomata in response to either stimulus, though control animals were able to respond to both. At present we are still trying to determine what changes the IUFB cause that prevent the development of normal uterine sensitivity and thereby inhibit implantation.

The difference in effect of the IUFB between rats and rabbits led us to think that similar studies in another rodent might be of interest, so we began a third set of experiments in mice. We felt that it was important to determine if two species which were closely related reproductively would react similarly to an IUFB.

The IUFB was placed in the same manner as in the rat, and the first group of animals was autopsied on various postimplantation days. In the 32 mice which had an IUFB in place at time of autopsy there were, as in the rats, no implantations in the operated horn; however, unlike the rat, 72 percent of the animals had also failed to implant in the control horn. Nine animals which did have control implants averaged only 3.5 sites per horn, compared to an average of 6.3 implantations per horn in a small group of controls bred at the same time to the same group of males. The findings in the mice also differed from those in rats in another way. Although these animals were autopsied after the time of implantation occurs in mice, about 10 percent of these animals had ova in the control horn, and another 10 percent had ova in the tube of the control side. The uterine ova from these animals were normal, but those ova recovered from the tube of the control side were not. Although we never found ova in the uterine horn with an IUFB in place, 41 percent of the females which we killed post-implantation had ova in the tubes on the operated side. Most of these ova were either uncleaved or fragmented, but 5 females did have normal blastocysts which, although they were still in the tube, had shed their zonae and were very similar in appearance to the ova recovered from the uteri of "delayed implantation" animals.

The data on animals which were killed prior to implantation do not help us to understand why there is such a low rate of implantation on the control side since the number of ova recovered is approximately the same as that found in unoperated animals of this strain. There is not a significant incidence of abnormality of the control ova except on day 3. It is most probable that this relatively high incidence of abnormal ova is related to the interval between the operation and the time of mating, since 4 of the 5 animals killed on day 3 had mated the night of the operation, when perhaps the uterus was not most favorable to sperm transport. We also could not find any positive information as to why the ova do not implant in the horn with the IUFB, but we can rule out that it is because they are nonfertile or abnormal. To account for implantation failure on the basis of abnormal ova, we would have to have the same proportion of ova abnormal on each day, but the proportion tends to decline. The rather high incidence of abnormality on day 2 might only reflect a slight retardation of cleavage. The most interesting thing found in the pre-implantation recoveries was that on day 4, while all the control ova were found in the uterus, the ova recovered from the operated side were all still in the tube.

Why the ova undergo "tube locking" on the sutured side, why there is an increased incidence of implantation failure on the control side, why the ova do not implant in the horn with the IUFB in mice, are just a few of the major questions that still remain to be investigated in mice.

It would seem then that the effect of an IUFB becomes more pronounced as we move from rabbits to rats to mice. In rabbits it is either ineffective in preventing implantation or effective only in the area circumscribed by its physical presence. In rats the area in which it inhibits implantation seems to be the horn, but only that horn, which contains it, while in mice it appears to block implantation in the treated horn, interfere with tubal transport of ova on the operated side, and perhaps impede implantation in the control side in lessening degrees.

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CONTRACEPTIVE EFFECT OF PLASTIC DEVICES IN CATTLE UTERI[†]

by

H.W. HAWK, Ph.D., H.H. CONLEY, B.S., T.H. BRINSFIELD, M.S., and
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This study was directed toward both applied and basic objectives: to investigate the feasibility of installing plastic devices in the uterus to sterilize cattle, and to obtain information on the mechanisms involved in any contraceptive action of such devices.

Experimental procedures

The cows were Holstein dairy cattle. "Experimental" cows were those used for work with intra-uterine devices. "Controls"were those used in testing fertility of the bull semen used to inseminate the experimental cows. Cows of both groups were inseminated artificially with frozen semen from the same bull.

The experimental cows ranged from three to eight years of age. Each had calved at least once, so their previous ability to conceive was known. They were all in late lactation, several months postpartum, and were not milked during the experimental period. None of the cows had been bred after the last calving. All were in good general health, had shown no purulent discharges from the genital tract since last calving, and had no abnormalities of the reproductive tract detectable by rectal palpation. Negative responses were obtained with each cow to tube agglutination tests for *Brucella abortus*, cervical mucus culture tests for *Vibrio fetus*, and agglutination lysis tests for *Leptospira pomona.*

The experimental cows were checked twice daily for estrus. In most cases a control estrus cycle was observed before devices were inserted into the uterus. The nature of ovarian function in each cow was ascertained by rectal palpation of the ovaries once or twice each week.

The devices inserted into cow uteri were made of polyethylene plastic in two general shapes: spiral and "loop." Spiral devices were made by winding strips of polyethylene around test tubes of the desired diameter and boiling. Loops (so-called because of their similarity in shape to the Lippes loop) were made by winding strips or rods of polyethylene to the desired size and shape around nails in a board and boiling.

In an initial test of intra-uterine contraception, small spirals were inserted into cattle uteri. Although these spirals were larger in diameter than the normal contours of the uterine lumen, they were often expelled from the uterus. Larger loops or spirals were used subsequently.

The larger devices caused considerable distention of the uterus and generally remained in place. Devices were inserted into both uterine horns of each cow.

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Insertions were made through the cervix under clean but not aseptic conditions. Aseptic procedures were not used, in order to simulate circumstances which would likely prevail if this practice were to be applied to large numbers of cattle.

With some exceptions noted later, the plastic devices were inserted into cattle during estrus, and the cattle were bred at most succeeding estrus periods.

Results and discussion

Effect of devices on fertility: Spirals or loops were in place in both uterine horns of 18 cows when the cows were killed after the last experimental breeding. These cows had returned to estrus after a total of 42 experimental services, with no evidence of conception in any cow. Each cow was bred again and killed a pre-determined number of days postbreeding. The only evidence of pregnancy was a three-day cleaving ovum recovered from one cow. This was thus the only possible pregnancy subsequent to 60 services, and it may be considered doubtful that a normal pregnancy would have ensued.

Fertility in the control cows was satisfactory; all 21 cows were pregnant after a total of 38 services. A comparison of the fertility of experimental and control cows is given in Table I. These data indicate that intra-uterine plastic devices were effective contraceptives under the conditions of this experiment.

TABLE I

Comparative fertility of experimental and control cows

Type of cow	Number of cows	No. pregnant at end of experiment	Total No. of services
Control	21	21	38
Experimental	18	1*	60

* A cleaving ovum was recovered from the oviducts of one cow 3 days post-breeding.

Mechanisms of contraception: The second objective of this study was to gain some understanding of the means by which intra-uterine devices might act as contraceptive agents. Five experimental cows with corpora lutea on the ovaries were killed between 15 and 19 days post-breeding to determine whether embryos were present in the uterus. This stage of gestation is more than two weeks before implantation in the cow. No embryos were found, which suggested that contraceptive effects were occurring before this stage of gestation.

It would be expected that under normal circumstances fertilized cleaving ova could be recovered from cow oviducts about 90 percent of the time at three days post-breeding. Nine cows were therefore killed at this time and the oviducts flushed to recover ova. A cleaving ovum of eight blastomeres was recovered from an oviduct of one cow, an uncleaved ovum was recovered from the oviducts of each of four cows and no ova were recovered from the oviducts or uteri of four other cows. Three cows with no devices in the uterus were also killed at three days; a cleaving ovum of eight blastomeres was recovered from the oviducts of each one. These data are given in Table II, and suggest that intra-uterine plastic devices in these cattle exerted most of their contraceptive effect within the first three days post-breeding.

It is probably of some significance that ova were not recovered from four of these nine experimental cows, since ova can ordinarily be recovered from oviducts of almost all normal cattle at three days post-estrus.[2,5] Even though the numbers of cattle are small, the data suggest that devices in the uterus influenced the pickup or transport of ova.

TABLE II

Effect of intra-uterine plastic devices on the incidence of cleaved ova in the oviducts at three days post-breeding

Type of cow	No. of cows	No. of cleaved ova	No. of uncleaved ova	No. of cows from which ova not recovered
Control	3	3*	0	0
Experimental	9	1*	4	4

*8 blastomeres.

It is also probably of significance that ova in four cows showed no signs of cleavage and were probably unfertilized. Ordinarily, ova from almost all cattle bred to bulls of high fertility are cleaving at three days post-breeding.[2,5] Thus, it appears likely that intra-uterine devices in these cattle interfered with fertilization of ova. It must be considered, however, that these cows were bred artificially with diluted semen, and the number of sperm deposited in the uterus at breeding may have been less than the number that would have entered the uterus after natural mating. Thus, if the plastic devices inhibited fertilization by interfering with sperm passage through the uterus, the incidence of fertilization failure could have been higher in these cattle than would occur under conditions of natural mating.

Part of the contraceptive effect of the plastic devices may have been exerted through an effect on ovarian function. The corpus luteum is ordinarily detectable by rectal palpation between about five and 18 days post-estrus during a normal estrus cycle of approximately 21 days. A detectable corpus luteum did not form during many of the estrus cycles of the experimental cows, indicating inhibition of corpus luteum development by the devices in the uterus (Table III). Also, it appears that the incidence of inhibited corpus luteum development was influenced by the size of device in the uterus; corpora lutea of palpable size failed to form in cows carrying large devices more often than in those carrying small ones. The failure of corpus luteum development would in itself cause the death of any embryos reaching the uterus, since the level of progesterone secretion would undoubtedly be insufficient to maintain pregnancy.

When corpus luteum formation did not occur (Table III), the estrus cycles tended to be short, usually between 7 and 13 days in length. The cows with large devices had a few longer cycles, which increased the mean cycle length for this group. It has been reported that various stimuli introduced into the uterine lumen inhibit development of the corpus luteum in cattle, and that in such cases the estrus cycle is usually shortened.[4] There is much experimental data concerning effects of the uterus on ovarian function both in large and small animals.[1]

Because a detectable corpus luteum did not form after a high percentage of estrus periods in cows with large devices in the uterus, a pertinent question is whether ovulation occurred in conjunction with the estrus. The best available evidence suggests that ovulation probably did occur in most cases; each of the nine cows with large devices *in utero* had freshly ovulated when killed at three days post-breeding, and it may be doubted whether normal corpora lutea would have developed in all of these cows. In fact, the possibility must be considered that initial effects of the intra-uterine devices on corpus luteum development could account for some of the reproductive failures found at three days post-breeding.

TABLE III

Incidence of normal corpus luteum formation following estrus

Type of estrus cycle	No. of cycles	Cycles with normal corpus luteum development following estrus	Mean length of cycles with normal corpus luteum development*	Mean length of cycles with abnormal corpus luteum development*
		(%)	(days)	(days)
Control cycles before insertion of devices	19	100	25	—
Cycles of cows with small spirals *in utero*	24	71	23	8
Cycles of cows with large spirals or loops *in utero*	28	43	25	16

* The terms "normal" and "abnormal" refer only to the size of corpora lutea as determined by rectal palpation.

There were some cases where it was known that ovulation did not occur after estrus. Four cows were killed while large cystic follicles were present on the ovaries following an anovulatory estrus. To the extent that ovulation failure may have been caused by plastic devices in the uterus, the devices acted as contraceptive agents by inhibiting ovulation.

In a study with Indian water buffaloes, it was found that intra-uterine plastic devices caused failure of corpus luteum development during most estrus cycles.[3] It was believed that ovulation did not occur in most instances.

Inflammatory responses to intra-uterine devices: No evidence of uterine infection was seen in any cows into which plastic devices were inserted during estrus. Devices were inserted into uteri of eight cows at times other than estrus. One of these cows developed a gross pyometra with a purulent discharge; three others had flakes of pus in mucous discharges at the first estrus period after insertion of the devices, but showed no evidence of infection thereafter. The purulent discharges were likely due to uterine infection subsequent to contamination of the uterus with vaginal bacteria during the luteal phase of the estrus cycle.

At autopsy, a thin layer of monocytic and polymorphonuclear leukocytes was adhered to the plastic device in most animals. In a few cows there was also a mild leukocytic infiltration of the endometrium in the area of the device. Edema of the endometrium was found in varying degrees of intensity around the devices. The most edematous endometria were found in cows killed soon after installation of the devices and in those with cystic ovarian follicles.

Summary

Eighteen cows with plastic devices in the uterus returned to estrus after 42 infertile services, indicating effective contraception. Each cow was bred again and killed before the next estrus. Four cows had not ovulated; five others had ovulated but were not pregnant at 15 to 19 days

post-breeding. Nine experimental and three control cows were killed three days post-breeding. Each cow had ovulated. A cleaving ovum was recovered from the oviducts of each control cow, but only from one of nine experimental cows. An uncleaved ovum was recovered from each of four experimental cows, and no ovum was found in oviducts or uteri of the other four cows.

Results suggested that most of the contraceptive activity of intra-uterine devices occurred within the first three days post-breeding.

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MECHANISM OF ACTION OF THE INTRA-UTERINE CONTRACEPTIVE DEVICE IN THE PRIMATE. I: TUBAL TRANSPORT OF OVA AND DISTRIBUTION OF SPERMATOZOA(a)

by

LUIGI MASTROIANNI, Jr., M.D. and CHUSRI HONGSANAND, M.D. (b)

The mechanism of action of the intra-uterine contraceptive device is a subject of continuing speculation. One popular concept is that it causes failure of implantation through some influence on myometrial or endometrial behavior. A few investigators, notably Margulies[3] and Tietze,[6] have suggested the possibility that the coil may influence reproductive processes at the tubal level, perhaps by causing rapid transport of ova into the uterus. The relatively low incidence of tubal pregnancy among patients using the device would seem to support this idea. The purpose of this study is to evaluate the influence of the intra-uterine coil on primate reproductive processes..

Methods and materials

Adult female monkeys (*Macaca mulatta*) of proved fertility were used.(c) Coils of the Margulies type(d) were cut to size and introduced into the uterine cavity *per vaginam.* It was found that the colliculus, a structure which protrudes from the anterior lip of the cervix into the cervical canal, could be bypassed easily and no difficulty with vaginal insertion was encountered. Superovulation was induced according to the system outlined by Simpson and Van Wagenen[5]. Human urinary gonadotropin(e), 550 units, was given intramuscularly daily for six days beginning on cycle day 5, followed by 275 units and 2000 I.U. of human chorionic gonadotropin(f), for three days in coil and noncoil (control) animals. Artificial insemination with specimens obtained from adult males of the same species was carried out daily during the last three days of gonadotropin treatment. The semen was obtained by electroejaculation.[1] After standing at room temperature for 10 minutes, the liquified portion of the ejaculate was introduced into the vaginal fornix, and the coagulum then inserted to act as a vaginal plug. Approximately 24 hours after the last ovulating injection, the abdomen was entered under *Sernyl* anesthesia(g). Ovaries were carefully inspected for fresh corpora

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(*d*) The authors would like to thank Dr. Lazar Margulies for supplying the coils used in this study.

(*e*) Generously supplied as *Pergonal* by Dr. Charles Thompson of the Cutter Laboratories, Berkeley, California.

(*f*) Generously supplied as *APL* by the Ayerst Company.

(*g*) *Sernyl* was generously supplied by the Parke-Davis Company.

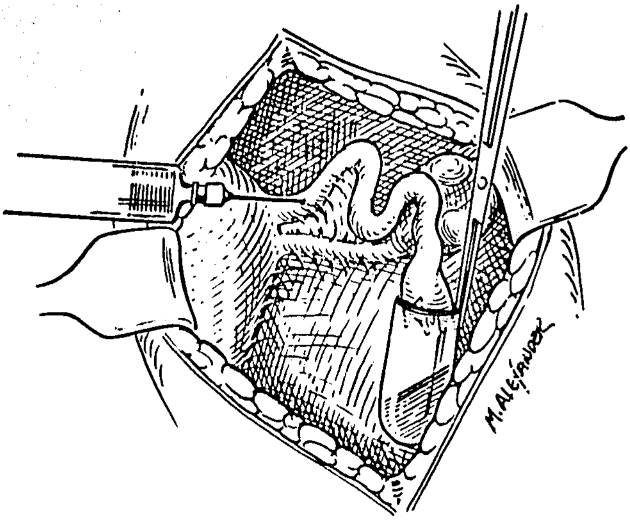

Fig. 1. Method for recovery of ova from the fallopian tube in the superovulated, artificially inseminated monkey.

lutea. Each fallopian tube was then flushed with warm Krebs-Ringer phosphate solution, using the method recommended by Hartman[1] (Figure 1).

The effluent was collected in plastic receptacles and inspected microscopically for the presence of ova and spermatozoa.

Results

In eight control (noncoil) monkeys, 21 fresh ovulation points were noted. Eleven ova were recovered, yielding a recovery rate of 52.4 percent (Table I).

TABLE I

Control (noncoil) series

Monkey No.	1	2	3	4	5	6	7	8	Total
*Rt. tube	2/2	0/2	2/2	2/3	0/1	1/2	0/1	1/2	8/13
*L. tube	1/2	0/1	0/1	1/1	0/0	1/1	0/0	0/2	3/8

* Ova recovered/ovulation points.
Overall recovery rate, 52.4%.

Seven coil monkeys were studied (Table II). Ova were recovered in one in which the coil was discovered to be lying free in the vagina. In the remaining six, the coil had remained *in utero*. There were 15 ovulation points; no ova were recovered. Spermatozoa were present in the tubal washings in four of six animals.

The absence of ova in the fallopian tubes of the coil animals could have resulted from failure of ovum pickup or from rapid transport of ova into the uterus. In an attempt to differentiate between these possibilities, a ligature was placed just beyond the utero-tubal junction on one side in a group of six coil animals. A similar protocol was followed. On the ligated side there were ten ovulation points; five ova were recovered (Table III).

TABLE II

Coil series

Monkey No.	C_1	C_2	C_3	C_4	**C_5	C_6	C_7	Total
Spermatozoa		+	+	+	+		+	
*Rt. tube	0/1	0/2	0/2	0/2	1/1	0/1	0/2	0/11
*L. tube	0/1	0/1	0/3	0/0	2/3	0/0	0/0	0/8

* Ova recovered/ovulation points.
** Coil in vagina; excluded from total.

TABLE III

Coil series

Monkey No.	C_8	C_9	C_{10}	C_{11}	C_{12}	C_{13}	Total
Spermatozoa	+	0	+	+	+	+	
*Rt. (ligated) tube	1/2	0/1	1/1	0/1	2/3	1/2	5/10
*Left tube	0/3	0/3	0/2	0/2	0/2	0/2	0/14

* Ova recovered/ovulation points.

On the unligated side there were fourteen ovulation points; no ova were recovered. Spermatozoa were present on the unligated side in five of the six monkeys.

Conclusions

Normally the ovum is retained in the fallopian tube of the primate for approximately three days before it is delivered to the uterus[1]. In the above experiments, laparotomy was carried out within five hours after the expected time of ovulation, judged to occur within 18 to 20 hours after the last ovulating injection. In the control animals, the ovum recovery rate was approximately 50 percent. Failure to recover more ova may reflect the technical difficulties involved in flushing the tubes *in situ*. Other possibilities are that not all of the ova released from the superovulated ovaries were picked up by the tubes, or that luteinized follicles were misidentified as ovulation points. Absolute confirmation of follicular rupture would have required oophorectomy and serial section. Among the coil animals not one ovum was recovered. Although the series is small, the difference between the two groups is very significant. The absence of ova could be explained in one of two ways: failure of ovum pick-up by the tube, or rapid transport of ova from the fallopian tube to the uterus.

Ovum distribution in the fallopian tubes of coil animals was studied further in a series of coil animals in which one fallopian tube was ligated at the uterotubal junction. Recovery of ova from the ligated side at approximately the same rate as in the noncoil animals suggested that the coil did not impair the mechanisms of ovum pick-up. Although extremely unlikely, the possibility that the effect of the coil was neutralized by placement of the ligature has not been excluded.

The presence of spermatozoa in the tubal washings from coil monkeys was expected. Spermatozoa have been recovered from the fallopian tubes of patients with coils in place.[2]

The evidence strongly suggests that in the Macaque the presence of an intra-uterine coil is associated with a rapid transport of ova from the fallopian tube. This occurs relatively shortly after the ova are picked up, probably within four hours or less. Several ova in the control series were still in cumulus, and four of five ova recovered from the ligated side in the coil group were in cumulus, suggesting that the transport of ova from the opposite tube occurred shortly after ovulation. It is not unlikely that ova are extruded before fertilization has occurred, but an assessment of the relationship between the rapid transport of ova and fertilization must await successful recovery of ova from the uterus or vagina in coil animals. Efforts in this direction are presently being made.

Summary

Intra-uterine coils were introduced *per vaginam* in adult female monkeys (*Macaca mulatta*). In coil and noncoil (control) animals, superovulation was induced with human urinary gonadotropin and human chorionic gonadotropin. Artificial insemination with electroejaculated semen was carried out daily during the last three days of gonadotropin treatment. Approximately 24 hours after the last ovulating injection, ovaries were inspected for fresh corpora lutea and the fallopian tubes flushed for the recovery of spermatozoa and ova. Among eight noncoil animals, the recovery rate was 52.4 percent. Among six animals with the coil still in place, there were 15 ovulation points; no ova were recovered. One animal in the coil group yielded four ovulation points; three ova were recovered, but the coil had been expelled. Spermatozoa were recovered from the fallopian tubes of four of six coil animals. The ovum recovery experiment was carried out after one fallopian tube had been ligated at the uterotubal junction in six coil animals. There was a 50 percent recovery rate in the ligated side in contrast to zero percent in the unligated side. Spermatozoa were recovered in five of the six monkeys from the unligated side. It would appear that, in the Macaque monkey, the presence of an intra-uterine device is associated with rapid discharge of ova from the tube into the uterus. Sperm migration remains unimpaired.

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ACTION OF INTRA-UTERINE FOREIGN BODIES: EXPERIMENTS IN THE RAT AND RABBIT

by

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By what mechanism does a foreign body in the uterine cavity inhibit pregnancy? A partial answer seems to have been found for some animal species. The first experimental work on this subject was done by Carleton *et al.*[1] in the rabbit. They simply concluded that mechanical action exerted on the mucosa by a foreign and inert body in the uterine cavity prevented implantation of the ovum.

We performed a series of experiments in rats and rabbits[3], and concluded that the contraceptive action could not be explained by a mechanical factor alone, but that some kind of endometrial inhibition operates. In the rat the reaction is general—it occurs throughout the uterus and perhaps even in the ovarium, where we have found also a partial inhibition of ovulation. In the rat the same kind of general reaction can be attained by autografting a piece of skin on the endometrium (Figure 1). In our experiments[4] the grafted epithelium grew to cover the glandular tissue and remained *in situ* without any alteration over a period of 4 months of observation (Figures 2 and 3). In the rabbit, however, the inhibitory response to a foreign body was confined to the area of contact. Experiments with autografts in the rabbit have not been carried out as yet. In humans, is it not known whether the response is localized, as in the rabbit, or general, as in the rat.

Malkani and Sujan[2] have demonstrated that sperms ascend to the tubes in ring wearers, but it is not clear whether fertilization of the ovum takes place.

Experimental removal of the ring one or two days after a fertile coitus, in order to establish whether or not implantation has occurred, seems not to have been done in humans as yet.

Assuming that the ovum can be fertilized with the ring *in situ*, the low incidence of ectopic pregnancies in ring wearers may be explained on the theory that there is an acceleration of tubal-uterine peristalsis. However, a general response that includes the tubes, as in our experiments with the rat, might also be an acceptable explanation. In the rabbit, if there is an acceleration of tubal-uterine peristalsis, it does not accelerate the expulsion of the blastocyte[1] (Figure 4).

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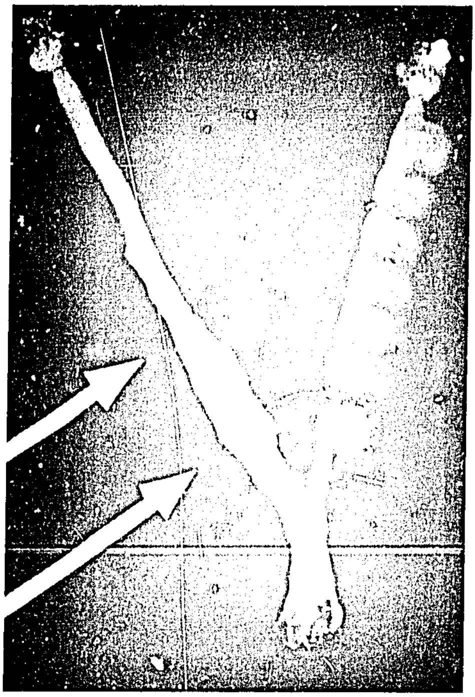

Fig. 1. Rat uterus, with skin autograft in endometrial cavity indicated by arrows.

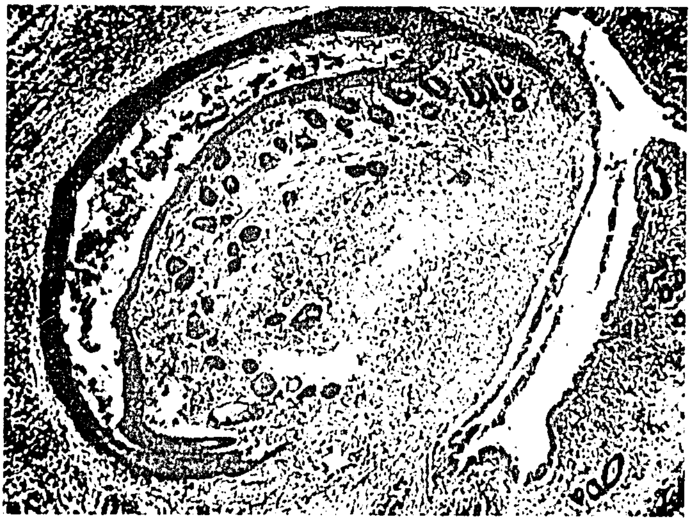

Fig. 2. Skin autograft covering glandular epithelium in rat uterus (low magnification).

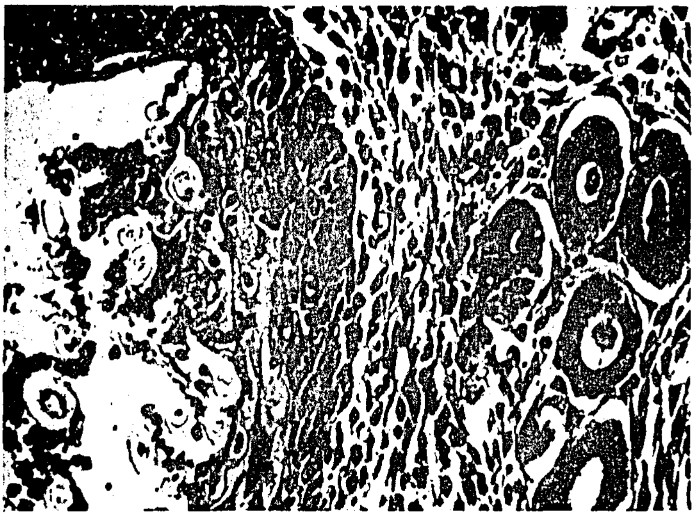

Fig. 3. Skin autograft covering glandular epithelium in rat uterus (high magnification).

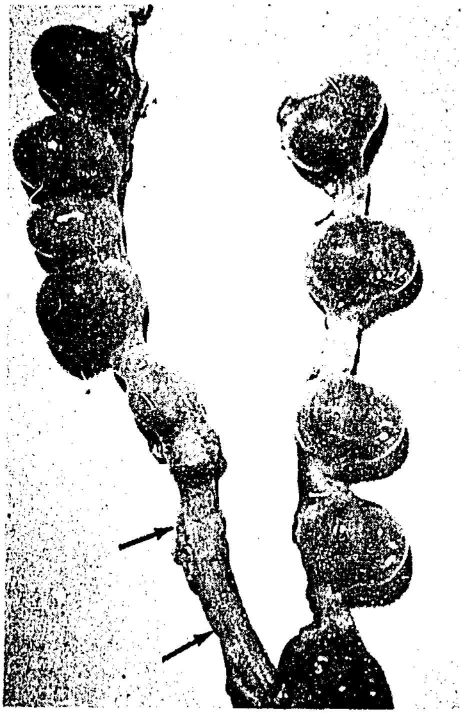

Fig. 4. **Pregnant rabbit uterus, with skin autograft in the endometrial cavity indicated by arrows.**

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DISCUSSION

Placement, size, and design of intra-uterine devices

DISCUSSANT (not identified): From Dr. Burnhill's experience with hysterography, I gather that he advocates that the device should be high up in the fundus. We had thought that this would leave free empty areas which would allow pregnancies. Would he please comment?

Dr. BURNHILL: When we advocate placement high up in the fundus, we mean that the major portion of the device should be located intrafundally. It is just that we feel that some failures are due to timid insertion of the device, which may then be ejected in the cervical isthmus junction or partially withdrawn, leaving the fundus unprotected. As Dickenson pointed out 35 years ago, 95 percent of pregnancies take place in the midline or up in the posterior portion.

DISCUSSANT (not identified): If a device is by accident placed intraperitoneally, is it mandatory to remove it or may it be left in place and in due time another intra-uterine device be inserted?

Dr. BURNHILL: I would be inclined to get a signed statement from my patient that she has been informed of this particular complication, and that I offered to remove it if she so wished, but personally I would leave it there.

Chairman TAYLOR: Dr. Davis's paper, of course, raises the interesting question of whether there is an optimum ratio between a device's size and the variable uterine area. This would raise great difficulties if a patient had to be fitted individually.

Dr. Jack LIPPES (Dept. of Obs. & Gyn., University of Buffalo, New York): I would like to congratulate Dr. Davis on his very fine paper and on having studied the INCON design related to uterine size. Another factor that I think is important in relation to expulsion rates is what I call the modulus of elasticity. I have measured the force needed to straighten out the different devices, and find it correlates inversely with the expulsion rates. This finding might be expected, because the device is extruded through the cervical canal, about 4 mm in diameter. I did not find any correlation between expulsion rates and weight of the different devices.

Dr. TIETZE: I want to point out that in the case of the loops and in the case of the spirals, the larger sizes are associated with a significantly lower expulsion rate. Concerning the removal rate for medical reasons, however, the differences between larger and smaller devices are not statistically significant. You cannot say that either the larger or the smaller models of the loop and spiral have a higher rate of removal for medical reasons; the rates are not significantly different.

Dr. L. MARGULIES (Dept. of Obs. & Gyn., Mt. Sinai Hospital, New York City): From my own experience I can say that the larger the device the better it works and the fewer pregnancies there are. There are also fewer expulsions. I have begun to test a coil that is a bit stiffer than formerly. In three and a half months there have been five expulsions of this stiffer device out of 300 insertions, instead of the 22 expected.

I do not think the mode of expulsion is quite as Dr. Lippes described. The uterus can't execute the complicated maneuver with the muscle to straighten out the device and expel it. In all the cases where the device has been found in the cervix, it was being expelled in bulk. Two factors are involved. Most of the devices are expelled during menstruation. We know that the isthmus of the uterus is hypotonic at the beginning of menstruation, and the fundus of the uterus contracts during the first two days. It's the combination of these two conditions that brings the device out, and the smaller it is the easier.

Dr. Davis also mentioned the necessity of filling up the endometrium in order to prevent pregnancies. I tried to insert two devices at the same time and even three, hoping that there would be fewer expulsions. I inserted two regular No. 5 coils in about 180 patients. Of these, two became pregnant with two devices *in situ*, which means that filling up the uterus does not enhance the contraceptive effect.

Dr. Frank Shubeck (Dept. of Obs. & Gyn., University of Oregon Medical School, Portland, Oregon): I am delighted that Dr. Davis is working on this. We also have been injecting silastic, an innocuous plastic, but not the bathtub caulking compound, since we have been injecting into living patients.

I would agree with Dr. Margulies that probably the expulsion of the device is effected by uterine contraction and cervical dilation, since the expulsion rate of the silastic is probably twice that of the Margulies spiral. However, I would disagree with him that the spiral can't be uncoiled when it is being expelled. When I first got into this I was fortunate in coming across a patient who had a complete double uterus, and I put silastic in one horn and the Margulies spiral in the other. They were both expelled—the silastic first. But the Margulies spiral was uncoiled as it came out. We first cut off about an inch of it and the next day we cut off another inch and a half. Finally it was completely uncoiled and came out this way.

Effect on milk ejection and on the menstrual cycle

Dr. Y. Sica-Blanco (Gynecology Clinic, Faculty of Medicine, Montevideo, Uruguay): In the very interesting work presented by Dr. Gomez-Rogers and his group, the important thing is the fact that oxytocin is modified by the administration of gestagens to the mother. I think that the treatment dose is a critical factor in this study—the administration of oxytocin intravenously in small doses of 0.5 or 0.2 mU is critical, and it is very important to relate the weight of the patient to the oxytocin administration.

I think that the intra-uterine device does not produce modifications in the response of the mammary gland, and physiologically the ejection of milk is a process in which the mechanical method would depend on the oxytocin. Similarly, the threshold dose is a factor not important in the interpretation of the results.

Dr. R. Richart (Dept. of Obs. and Gyn., College of Physicians and Surgeons of Columbia University, New York City): I would like to make one comment on the paper on the effect of intra-uterine devices on the menstrual cycle. I wonder if some of the so-called active cells which were reported and the polymorphonuclear leukocytes and lymphocytes may not be accounted for by necrosis rather than infection? We have seen a number of cases, particularly those using fairly large devices, in which there was necrosis where the device impinged on the lateral portion of the endometrial cavity. In one case there was regeneration with active-looking cells, which is simply an effect of the necrosis rather than infection *per se*.

Dr. Vorys: I am sure we would agree with that.

Chairman TAYLOR: I would like to ask Dr. Vorys one question. I think we are trying to set up hypotheses for these devices, and I was not certain whether or not the speaker believed from the evidence that he has at hand that the devices induce an endocrine disturbance, and if so, what it is.

Dr. VORYS: This material, of course, was collected on four patients, which is a restricted group to say the least. We tend to believe that the menstrual cycle in the first four or five months is disturbed if the device is in place. It probably alters the quantity of FSH and LH. We feel also that the corpus luteum phase of the menstrual cycle was shortened in several of the patients on whom we had gonadotropins. We thought that the incidence of anovulation was not particularly high in this group of people. I feel that it is important to measure urinary estrogens as well as serial pregnandiols to rule out the possibility of hyperestrogenism in these menstrual cycles with the coils in place.

Pathology

Chairman TAYLOR: We have had three reports concerned to a considerable extent with the attempt to determine whether intra-uterine devices produce inflammatory changes in the endometrium, and if so, precisely what their nature is. This very important subject is now open for discussion.

Dr. Lee B. STEVENSON (Dept. of Obs. and Gyn., Henry Ford Hospital, Detroit): I would like to ask Dr. Moyer whether his cultures were correlated with the menstrual cycle?

Dr. MOYER: Yes, they were. Approximately half were done in the proliferative phase and the other half in the secretory phase. We have certainly found an increased number of positive cultures in the proliferative phase as opposed to the progestational phase, just as other investigators—particularly Dr. Willson's group—have noted.

Dr. A. SEDLIS (Dept. of Obs. and Gyn., New York Medical College): I am addressing my comments to both Dr. Willson and Dr. Moyer. I would like to comment on the criteria of infection and inflammation *in utero*. Dr. Moyer thinks that lymphocytic aggregates or lymphocytosis are signs of inflammation. I have seen this occur in the normal uterus. I wonder if lymphocytic infiltration was noted, because this may be a sign of involution, which we have observed to exist as long as three or four months.

Further, the presence of leukocytes in the gland lumen is not described as a sign of endometritis in any of the classical textbooks. I think that you have to interpret them very cautiously.

Dr. Hans LEHFELDT (Dept. of Obs. & Gyn., New York University Medical Center): The difficulties of making a diagnosis of endometritis and bacterial infection of the endometrium have been very well evaluated by the investigators who have spoken. We have compared endometrial biopsies and endometrial cultures on 250 patients with the Hall-Stone device and the Lippes loop.

The cultures did not give us any clue as to the presence of infection of the endometrium. As a matter of fact, we had more positive cultures prior to insertion than after. Endometrial biopsies also failed to show significant differences before and after insertion, and we did not find any difference between the device with the appendage and the wholly intra-uterine device.

An additional factor I want to mention in connection with the group associated with Dr. Willson is that if endometritis is found in the neighborhood of an intra-uterine device in a hysterectomy specimen, one has to consider the probability that these devices were inserted in patients who had uterine pathology.

Dr. Herbert HALL (New York Medical College): We have been carrying out a study on women in the child-bearing age who had been fitted with the intra-uterine steel ring. The protocol was set up so that biopsies were taken before and after insertion on a definite date of the cycle for each patient, so that the results could be compared with the least danger of a coincidental finding confusing the picture, particularly as far as the dating of the specimens was concerned.

We also were concerned with any evidence of endometritis. Applying the criterion of the presence of plasma cells, we failed to find any evidence that there was endometritis in the presence of the ring. In 91 patients we found five pre-insertional specimens that showed plasma cells, but nowhere nearly in the numbers that Dr. Willson requires for his diagnosis, and only two of those persisted in the postinsertional specimens; none continued further on in the study: we had none after three, six, and nine months of the ring *in situ.*

We had no evidence of pyometritis or effect on the endometrium in ten cases of hysterectomy where the device had been *in situ* for as long as thirteen weeks preoperatively in women who were free of uterine pathology and who had hysterectomies for prolapse.

Even though Dr. Lehfeldt found no difference between plastic and stainless steel in the incidence of pathology in his cases, I would like to make a plea that investigators try to compare their results not only with a view to design but also material. It is entirely possible that the differences in the incidence of such complications as infection, pelvic inflammatory disease, and bleeding that appear in the statistics that Dr. Tietze showed us may be due to a difference in the quality of material employed as well as the design of the device.

As for any effect on the cycle, we have none to report. There was no difference in the data that would indicate any shift in the secretory activity of the ovary or the response of the endometrium in the presence of the intra-uterine ring.

DISCUSSANT (not identified): In Brazil the intra-uterine devices are used very seldom, mainly because they are not available for doctors to prescribe them. In the Brazilian community contraception is carried out conventionally. However, during the last four or five years the oral contraceptives have come into wide use, and I feel sure that they will soon be used more than diaphragms, jellies, and so on.

But another reason that restricts the use of intra-uterine devices is fear of uterine cancer. I am tempted to do an experiment with the use of the plastic intra-uterine device, but I feel we should have more histological data upon this very special and very important problem, the prevention of cancer.

Chairman TAYLOR: This is an important subject. I think when we discuss it we should be careful to distinguish carcinoma of the endometrium and cancer of the cervix, and I judge that when we are talking about direct irritation as a possible factor in the etiology of cancer we are talking about cancer of the endometrium.

There are several points about this that should be remembered. The most important one is that cancer of the endometrium rarely occurs before the menopause. When it does occur before the menopause it is usually preceded by episodes of irregular cycles, strongly suggestive of an ovarian dysfunction as one of the predisposing causes.

One of the reasons advanced for its rare occurrence before the menopause is that if a pre-cancerous lesion starts, it presumably is sloughed off with each menstrual period. I should think that so far as cancer of the endometrium is concerned, this is a most unlikely eventuality, first because the disease is very rare before the menopause, at times when the device would be used; secondly, because all the evidence is that cancer of the endometrium is not produced by local irritation but by some constitutional, perhaps endocrine, cause. So that the risk of endometrial cancer is most unlikely on the basis of our knowledge of this disease.

Dr. PINCUS: I would like to congratulate Dr. Taylor on his summary of endometrial cancer.

Experimentally this can be induced in animals by carcinogens, and one of the most interesting of recent developments in this area is that with manipulation you can inhibit the development of endometrial cancer due to carcinogens.

In this connection it is very interesting that among patients in Puerto Rico and Haiti who have been studied by us and from whom we have taken approximately 4,000 endometrial biopsies in the course of some years, the incidence of endometritis runs from 5 to 10 percent (depending on the locality) and the incidence of cystic glandular hyperplasia about 9 percent.

The latter particularly is considered by some pathologists as pre-cancerous. In women using the hormonal contraceptives the occurrence of both of these conditions is moderately reduced. I was very glad to notice that there has been no increase or only a very slight increase in endometritis in patients using intra-uterine devices.

I should like to ask, particularly of Dr. Moyer, about the incidence of cystic glandular hyperplasia of the endometrium, and also if anyone has data as to the effects of the intra-uterine device on this condition if it is pre-existing.

Dr. MOYER: I would only say that the results of our study have been limited to about six months' observation, and within that period of time we have not noted any abnormal hyperplasia nor cystic hyperplasia, nor have we noted any of the squamous metaplasia that our colleague noted previously.

Dr. MARGULIES: I think that it is right and correct for these histological, bacteriological, and other studies of the endometrium to be made. However, I would like to caution against undue anxiety concerning these studies and their interpretation.

We have had ample opportunity now since 1900 to observe the effects of metallic and plastic intra-uterine devices, and we must realize that these are laboratory findings but that clinically no such anxiety exists nor should it exist.

Recently I came across two cases who had intra-uterine devices put in 40 years ago. The women were unaware that they had them and only came because of a chronic discharge. The old devices were removed, and endometrial biopsies revealed that there was nothing to be concerned about; there was no evidence of malignancy or anything else outside of chronic inflammatory changes.

I would also like to point out that intra-uterine devices are available for inspection, whereas plastic devices such as are put in the heart or in blood vessels are not susceptible to frequent observation, but these also have similar inflammatory changes, as has been seen in animals. The inflammatory changes which result from steel sutures or from non-absorbable sutures are more or less the same. The inflammatory changes which occur with the plastic device are so little different from the inflammatory changes which occur normally in menstrual cycles that we should not let anxiety inhibit our enthusiasm for these devices, which are an enormous contribution to fertility control.

Please remember that these inflammatory changes are changes which also exist with other devices in any part of the body, but we as gynecologists should not be too frightened because we see these changes more often.

Dr. A. **Netter** (Collège de Médecine des Hôpitaux de Paris, France): First, did Dr. Willson or Dr. Moyer study the gradient of sensitivity to the device from the body of the uterus to the part which is in the cervix?

The second question is, did they study the correlation between the clinical symptoms and the histopathology? From the photographs which we have seen, there is mainly a purpura of the endometrium and perhaps in studying the fragility of the capillaries and from studying the allergy to the substance of the spiral, we could forecast the accidents. Did they study those two matters?

Dr. Moyer: In answering the questions in general, I would like to make a remark on Dr. Hall's comment that not only a study on some of the materials used in these pelvic loops is very important, but also I think one of the big differences between our series and a number of the others within the group is possibly the time at which the cultures were taken.

As a number of investigators have noted, some of the clinical indications of inflammatory disease are more prevalent within the first month or two. Our histological slides were also taken within this period of time. I believe this is one of the reasons why we have seen possibly more severe reactions and possibly more reactions in our patients.

I would also like to point out that I am the first to say that I don't know what stromal lymphocytosis and sub-epithelial accumulations represent. We have said that it must be understood that at the present time the exact significance of these morphological changes is not known. We were only pointing out these changes and abnormalities, and then hoped that our group and other groups might go on to make bacteriological studies and biochemical studies.

In correlating the clinical symptoms and some of our histological findings, Dr. Mishell has not found any overt clinical symptoms, particularly those outlined by Dr. Tietze yesterday, which might be indicative of a pelvic inflammatory disease. We have seen no cystic or adenomatous hyperplasia in any of our material. However, I would only caution that we have a relatively short experience in this field and we would like to refer that question to those people who have looked at more cases.

Dr. Willson: We also haven't seen any evidence of hyperplasia in the tissues that we have studied. I am not at all convinced that the changes that we have reported actually represent endometrial infection. I think the next step that has to be taken in evaluating these changes is to determine by histochemical studies of some sort whether or not this does represent infection, or whether it is an irritative change of some sort secondary to the presence of the device.

Dr. Sujan: We haven't found any endometrial hyperplasia in our two years of experience.

Dr. Ishihama (Dept. of Obs. and Gyn., Iwate Medical College, Japan): I am very happy to have a chance to present my own experience. At the request of a doctor in Japan, I made smear tests on a series of women. We unexpectedly found 72 women who had been wearing intra-uterine contraceptive devices for periods varying from one to ten years, or an average of 3.1 years. We found not one positive smear among these cases.

Dr. Pincus: I have some data on the Papanicolaou smears of patients using various contraceptive methods. These groups initiated the use of the particular method at approximately the same date. With the intra-uterine device, those having positive anaplastic smears after a period of two years is about 8 percent; after a period of less than two years, 7 percent, and so on. With the intra-vaginal methods—primarily foaming devices—the figures are not too reliable because of the smallness of the group, but the percentage goes up to about 10. In the case of *Enovid*, in which the numbers are a little larger in terms of patients, these run to about 5 percent.

This suggests what we have previously noted, that progesterone-estrogen combinations tend to suppress these types of anaplastic smears, whereas other methods apparently do not. We do not have any adequate controls with women who are not using contraceptive devices.

Dr. Herbert HALL (Dept. of Obs. and Gyn., New York Medical College): I would like to ask Dr. Pincus if these figures can be accepted if we do not know the age and profession of the various groups and the parity?

Dr. PINCUS: These groups were matched as well as they could be matched for age, parity, and so on. By and large, the users of the intra-uterine devices were younger women than those using the oral contraceptives, but the average age was not much less. They were mostly using the Lippes loop.

Dr. RICHART: I would like to encourage a good deal of caution in interpreting any figures dealing with incidence of cervical neoplasia that do not deal with extremely large numbers. It is extremely difficult to attempt to draw any conclusions based on 200, 300, 500, or even 1,000 cases. There are innumerable pitfalls that can make any such series completely meaningless. Each laboratory must know its usual false negative rate; this would vary with the laboratory, with the screener, and indeed with the man who takes the smears. The false negative rate is something which can vary, according to reports in the literature, anywhere from 2.5 percent up to 20 percent. It will vary enormously depending on the type of smear that is taken. For example, with a scraping and endocervical aspiration, the false negative rate is usually lower than if one uses the vaginal pool. If one changes personnel in the middle of the series, or the type of smear, this virtually negates the previous data that has been collected.

One also needs to know incidence figures for this lesion. To my knowledge there are no incidence figures available for dysplasia. I have corresponded with most of the people who are in the larger community screening programs, and none of them have incidence figures. It's extremely difficult to compare incidence figures with a control population since there are no control incidence figures currently available. I am surprised at the cumulative incidence rate of 4.6 percent shown in Dr. Pincus's series, since our prevalence rate in a symptomatic gynecological population of dysplasia only runs 3 percent.

We are currently attempting to accumulate a series of 10,000 women who will be screened cytologically prior to the insertion of the device, and we intend to follow these people for at least three years. According to Dr. Tietze, it has been calculated that it would require at least 10,000 women with a very well controlled cytological series followed for a number of years before one can detect even a doubling in the incidence rates, if indeed we can find normal incidence figures for the lesion.

Mechanism of contraceptive action

Dr. W.A. BONNEY (Dept. of Obs. and Gyn., Vanderbilt University School of Medicine, Nashville, Tennessee): We have done timed hysterectomies on some ten patients using the intra-uterine coil. At the time of hysterectomy we have also performed unilateral salpingectomies.

In these ten patients we have recovered two ova, one of which we believe is fertilized. These cases were done on the fifteenth and sixteenth day of the cycle.

Dr. MASTROIANNI: This is very exciting indeed, but I think a note of caution is indicated here. We know that rats are not rabbits and rabbits are not monkeys and monkeys are not people and there may be a difference, although this would surprise me because of the extreme similarity in reproductive cycle of monkeys and people. I would ask you, Dr. Bonney, what the evidence was that this ovum was fertilized and, secondly, how about the time relationship to actual ovulation? Were you able to obtain a specimen from the corpus luteum in order to assess its duration or viability?

Dr. BONNEY: In one case we were. In the case of the ovum that we believe is fertilized, we were not able to obtain the corpus luteum. We have a slide showing, we believe, a pronuclear ovum containing the nucleus. Unfortunately, the corona radiata, because of the fixation, has been lost. (*This refers to a slide that was shown, but not reproduced here. Ed.*) In the middle of the field I think you can see a structure which we believe is the spermatozoon that actually fertilized this ovum. We can identify the tail and the midstructure and we think the neck but not the head.

Chairman TAYLOR: I am going to ask Dr. Witschi if he will comment on the histology.

Dr. E. WITSCHI: It certainly appears to be a pronuclear ovum.

Dr. MASTROIANNI: Dr. Bonney, there are one or two comments. I think it would be important to know how long the device was in place before the tube was flushed. Secondly, when the histology of this fallopian tube was studied, was there any evidence of a chronic salpingitis or something which may have prevented transport of the ova down the fallopian tube? As you know, ectopic pregnancies occur among patients wearing the coil, and it is my feeling that in a large majority of patients who have ectopic pregnancies there is tubal disease which might have interfered with the mechanism.

Dr. BONNEY: Both cases have worn the device for approximately four months. In both cases fallopian tubes were normal.

Dr. M.C. CHANG (Worcester Foundation for Experimental Biology, Shrewsbury, Mass.): First I would like to congratulate my dear friend Dr. Mastroianni. It was a delightful presentation.

The second thing I would like to say is about Dr. Bonney's slide. In my judgment, it is definitely a fertilized egg. Then what I would like to mention about Dr. Mastroianni's work is that so far as the mechanism of this device is concerned, the evidence supports the theory that there is interference with transportation of the egg, but whether the egg is transported too fast into the uterus is still a question.

Dr. MARGULIES: I want to congratulate Dr. Mastroianni for his brilliant experiment and the proof that the prevention of pregnancy with intra-uterine devices is due to increased peristalsis of the tube during ovulation.

The egg in Dr. Bonney's slide is definitely fertilized, but from the study of the abstract I see that he has been inserting small coils, and this, just as a speculation, could possibly be one of the failures where the patient becomes pregnant with the device *in situ*.

In all statistics it was shown that the small spiral loop and small bow have much higher pregnancy rates. Therefore a warning for the future: insert as large a device as you can.

Dr. **Bonney**: The other egg was not fertilized. I add that in 70 cases we have had no pregnancies, but only this one fertilized ovum.

Dr. Herbert **Hall**: If the experiments of Dr. Mastroianni are applicable to humans, I think we also ought to examine other animal experiments, especially those of Dr. Margulies and Dr. Doyle and Dr. Delgado, who have shown that the placement of an intra-uterine foreign body in the rabbit and rat will not prevent pregnancy in the entire cavity but only in that part of the horn which seems to be occupied by a critical quantity of the device. So that this would indicate that the effect is directly on the endometrium rather than on the tube. I'm sure that the evidence on monkeys is very convincing, but it does not apply to the human race.

Dr. **Mastroianni**: Yes, I think it's terribly important to recognize that there are species differences. However, it is just as invalid to contend that lower primate observations do not apply to the human as it would be to insist that they do. We have established a mechanism in the monkey which, if applicable to the human, would account for the contraceptive action of intra-uterine devices. It remains to be determined by careful observation and experimentation if the same phenomena prevail in higher primates.

Dr. Peter **Eckstein** (Dept. of Anatomy, The Medical School, Birmingham, England): I, too, would like to express my congratulations to Dr. Mastroianni on his remarkable achievement. However, has his experiment been representative of the normal situation with the coil *in situ*? He has produced between two and three if not more ovulations from two ovaries by means of his superovulation treatment, and apart from everything else this will increase the amount of estrogen and progesterone produced by the ovary somewhat. Has he any comments on this?

Dr. **Mastroianni**: Yes. After all, we did treat these animals in a distinctly different way. The reason for our approach was that we wanted to be sure to recover eggs if they were around to be recovered. But it should be pointed out that in the non-coil series—and there were eight animals in this series—the recovery rate of ova was 50 percent. I don't know how many of these monkeys would have proceeded on to normal implantation. So that in a sense I think Dr. Eckstein has a valid point, but nevertheless, we are comparing two groups of animals treated in exactly the same way, except that in one group an intra-uterine device was in place; in the other group it was not, and there were clear-cut differences in ova recovery between the two.

Dr. R. **Delgado Garcia** (Univ. del Valle, Faculty of Medicine, Cali, Colombia): I think that Dr. Mastroianni's comments on the species differences are very important. In 1962 we carried out some studies on rats and rabbits. As far as the rat is concerned, we found that some fertilized ova were found in the tube at the right moment; in the rat the intra-uterine device was preventing implantation. In the rabbit the result was different; it was a local action with some implantation in these animals. It is true that monkeys are nearer human beings than rats or rabbits; on the other hand some reports indicate that with women there are pregnancies with the device *in situ*. We must keep in mind that we're not able to extrapolate from one species to another.

Dr. **Mastroianni**: We have stated several times during this conference that the incidence of ectopic pregnancy in the coil population is much less than would be expected. I think it is very important at this point to examine very carefully the fallopian tubes in which the ectopic pregnancies were lodged, because it's very possible that these cases were associated with intra-lumenal tubal disease, which can be pointed to as a major causative factor in ectopic pregnancy.

We know that ectopic pregnancies do occur in the absence of intra-lumenal tubal disease, and perhaps in some cases the intra-uterine device brought about more rapid transport of ova and, therefore, in a sense prevented ectopic pregnancy.

Dr. S.J. SEGAL (The Population Council, New York): With respect to experimental animals, especially the rat, it certainly seems quite likely that fertilization occurs, but that the contraceptive effect does not depend upon the inability of a decidual reaction to occur.

Like several other laboratories, we have confirmed the observations of Doyle and Margolis. We have tried to recover ova in the uterus after they leave the tube but before implantation. After the ova leave the tube, that is between day 3 and day 4, you can no longer find the ova. So that it would seem to me that the critical event may occur prior to decidualization.

Dr. PINCUS: I think it would be interesting to propose a general hypothesis. So far all the evidence suggests to me that we are dealing with a state of hyperestrogenism in animals fitted with intra-uterine devices.

I think it was in 1932 that I pointed out that ova in the monkey became tube-locked as a result of hyperestrogenism. You've heard about this phenomenon. Secondly, it's known from the work of Dr. Yoshinaga in our laboratory that there would be a local hyperestrogenism induced in any portion of the rodent uterus that you care to study. Thirdly, that the action in some of these species, particularly on the corpora lutea, is very clearly an indication of the inhibition of corpus luteum function and formation, which has been shown experimentally in many animals given an excess of estrogen.

Finally, in the rabbit, where we see implantation does take place, estrogen is one of the poorest inhibitors of implantation in contrast to the other species. So that by and large this would appear to me to be a tenable hypothesis.

If this is the case, it would be extremely interesting in these species to make a comparison between the action of estrogen and that of the intra-uterine foreign bodies— and some day estrogen may be substituted for the devices!

Dr. WISHIK (Pakistan): I am going to take the liberty of speaking at second hand about someone else's work. This is unwise, but the work is of sufficient interest to merit comment.

Dr. Moore of the University of Indiana, working in Pakistan and in Indiana, did studies on the bicornuate uteri of sheep. He inserted into one horn a balloon-like object which he distended with air so that it filled the horn and simulated an embryo. According to his reports to me, the opposite horn of the uterus could not hold an embryo, and the animal didn't become pregnant.

He then took this cylindrical horn and resected it by cutting it at both ends and removing all nerve connections. He then reversed it, inserted it and sutured it back into place so that the cylindrical shape of that horn was restored but presumably the nerve control still remained severed.

At this point the animal did accept a pregnancy in the opposite horn. What this experiment does not do is indicate what the mechanism is. What it does suggest is that there is at least a neurogenic factor or possibly a neuroendocrine factor.

Miss DOYLE: I have one comment bearing on Dr. Pincus's hyperestrogenism theory. We thought of this possibility too. It seemed unlikely in the rat because of the systemic factor that they were implanted in the other horn, but just as a further control in a small group of animals I removed the ovaries following breeding and substituted progesterone to maintain the blastocysts. Then they had no endogenous supply of ovarian estrogen, and on day 5 I added a small amount of estrogen. This is the traditional way of inducing implantation in castrated animals, and I found that implantation took place in the control horn as usual but did not implant in the horn with the foreign body.

I have one question to ask of Dr. Hawk. Did you put the devices in cattle at any particular time of the cycle, and if so, was this correlated with the incidence of abnormal cycles?

Dr. HAWK: Most of these devices were put in the cattle while the cattle were in estrus. In eight animals they were put in during the early luteal phase. In one animal where it was put in during the luteal phase we got a gross infection with a purulent discharge, which we might have expected. In three others we got pus and mucus discharges during estrus but nothing thereafter. There did not seem to be any relationship between the time that we inserted the devices and ovarian function, except that when we did put them in at estrus there was often an effect on that cycle. When we put them in in the luteal phase they did not affect that cycle but they did affect subsequent cycles.

Dr. S. SEGAL: With reference to possible neurogenic involvement, one of our students at The Population Council's laboratory, Mr. Parr, is studying the possible role of neural factors in IUFB-induced sterility in the rat. He has succeeded in achieving normal implantations in the horns of rats having intra-uterine foreign bodies exactly similar to the ones you saw today. He does this by severing the sympathetic nervous connections to the horn that has the IUFB in place. So we are very strongly on the trail of possible neurogenic involvement, at least in the rodent.

Dr. WISHIK: Discussion of the exact point at which intra-uterine devices exercise their contraceptive effect is bound to involve some examination of terminology. This is not merely an academic question. In a Moslem country such as Pakistan, if it is considered that the intra-uterine device is an abortifacient, this obviously would have a bearing on national acceptance or rejection of the method. I think, therefore, that careful attention should be given to a definition of terms.

I do not think it necessary for us to change the traditional definition of conception as being the point of fertilization, but the definition of abortion seems to be one that needs to be considered. Abortion, as the prefix indicates, means that something is taken away, and the taking away of an embryo which has successfully implanted itself would seem to be abortion. This has basis in the fact that we know in human beings a certain percentage of fertilized ova seem to be extruded through the uterus without there being any obvious pathology. Some of them implant and some of them do not, and we do not consider that an abortion has occurred because the fertilized ovum fails to rest in the uterus.

Dr. TIETZE: Yesterday I had opportunity to report on 142 intra-uterine and seven ectopic pregnancies with the device *in situ*. We therefore know very well that some ova are fertilized in the presence of the coil. But until we have more evidence that this is a usual event we should be very careful in stating that this is a mode of action of the intra-uterine device, and not disturb those people for whom this is a question of major importance.

Dr. MASTROIANNI: The philosophical question as to whether or not the ova are fertilized among patients wearing the intra-uterine device has certainly been stressed. I think this is worthy of just two comments.

At the conference today we have seen one human fertilized ovum. This was fertilized. However, there is no way of knowing what would have happened to this ovum if it had been allowed to reside in the fallopian tube and had eventually been transferred into the uterus. We do know that among patients wearing the contraceptive device, both ectopic and intra-uterine pregnancies, which incidentally go to term, are entirely within the realm of possibility. So that we can't really extrapolate from the fact that we have recovered one fertilized ovum in a fallopian tube and extend that to the point where we must assume that the ova in general are fertilized among people wearing the intra-uterine device.

Among the monkeys studied in our laboratory there is one point which I did not stress because at the time I did not think it was terribly relevant. Obviously, in the monkey the only way to know whether the ova are fertilized is to recover them. We can't find them. However, among the group of monkeys in which the fallopian tube was ligated on one side, we did recover ova. All but one of those ova were still in cumulus; they were not yet denuded down to the level of the corona.

On the other side no ova were recovered whatsoever. In this group of monkeys a laparotomy was performed at such time as we would expect to see ova, if they were available in the fallopian tube for fertilization. I think that in general when the ova are still in cumulus, fertilization may not quite yet be possible. Certainly fertilization is possible once the cumulus cells are dispersed and the corona radiata remain. So that whatever little evidence we have in the primate would suggest that the ova are extruded from the fallopian tube prior to fertilization.

Chairman TAYLOR: It has been suggested that we ought to set our definition that pregnancies start at implantation. I think it ought to occur to us that we are talking about a theological definition, not a biological definition, and this group can't possibly help in making this definition.

Dr. TIETZE: I would like to take issue with the chair on what I hope has not been a definitive theory.

I fully agree with you, sir, that the time at which a human life or any life begins is a philosophical question, but I submit that throughout history the theologians and the jurists have always taken into account and have listened to the prevailing medical and biological consensus of the times, and I think this is still true. If a medical consensus develops and is maintained that pregnancy, and therefore life, begins at implantation, eventually our brethren from the other faculties will listen.

SUMMATION

by

ALAN F. GUTTMACHER, M.D.*

So much has transpired in these two days that to summarize it adequately is an impossible task. However, it seems to those who were privileged to be at the first conference two years ago that rarely has so much been done in so short an interval.

The Population Council first became interested in intra-uterine contraception early in 1962. What has been accomplished by this large and very well-qualified audience in this two-day program is a tribute to what a thoughtful, well-financed organization can do in this area.

We now realize that the world has two effective methods of conception control, the oral progestins and the intra-uterine devices. Even if Dr. Pincus were not present, I should have given recognition to the importance of the orals. They have a very real place in global population control; with the narrow focus on intra-uterine devices at this conference we have neglected to put oral contraception into its proper perspective. In some Catholic countries with great population pressure, the orals will soon find favor by the Church. One will have to wait a long time for intra-uterine devices to have similar status. On the other hand, there is no question that in some parts of the world where there is great population pressure, and in our own country among the least privileged elements, where motivation for family planning is limited, the IUCD's have tremendous and pertinent application.

This two-day session has demonstrated that our task is well begun, but still there is a great deal to do. Some very simple questions remain unanswered. For example how do you train doctors, and how long does it take? What is the role of the general practitioner in this field? Can we employ paramedical personnel with reasonable safety? How early in the post-partum period can these devices be safely and effectively inserted? How frequently should patients be seen after insertion? What are the contraindications to the use of these devices? Should they be tailed or untailed? Should they be made of polyethylene or stainless steel? What should be their shape? Are the IUCD's going to substitute for surgical sterilization, as Dr. Williams from Jamaica suggested? What is the significance of the type of endometritis commonly seen with these devices?

Yesterday in our sociologic discussions we learned that the intra-uterine devices differ significantly from other types of contraception by their very high acceptability factor. When offered choice of several methods of contraception more than 70 percent of women choose this method because they want a single procedure that gives long-term and reversible protection against pregnancy. The speed with which the news of this technique travels indicates that women of different national backgrounds, economic levels, and parities clearly recognize the vast advantages of this method over all others in terms of the patient's and her spouse's convenience.

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* President, Planned Parenthood/World Population, New York City.

As a result of the high acceptability of this very effective technique, it seems to me that we may look forward to a reduction in the population growth rate in certain areas long before the socio-economic changes which accompany large-scale industrialization normally show their influence in depressing birth rates.

We were told that in the past month 11,000 women in Korea had the devices inserted, and in the next five years it is hoped and planned that a million women, in this country with a population of 30 million, will have these devices introduced. We were told that 4,000 women in Taiwan had the devices inserted last month, and that in the next five years 600,000, in a country of 12 million, will have them inserted.

Many questions remain on the administrative aspects of such birth control programs. The question of how many patients a well-qualified physician can serve was not touched upon, but I understand from people who work in the field that a well-qualified physician can take care of 50 to 65 patients in the course of one day. Another question concerns the relative merits of mobile units and fixed installations. These and many similar problems need further investigation and clarification.

The second part of this conference has been particularly interesting to me as a physician. From Dr. Tietze's discussions yesterday and further discussions today we cannot fail to agree on the extraordinary effectiveness of this method of conception control. I was delighted to learn today that the presence of intra-uterine devices has no effect on lactation. In those parts of the world which need population control most, lactation is an absolute essential for survival of the infant. Since the orals inhibit lactation in some, they cannot be used among nursing women, but not so the intra-uterine devices.

It is certainly heartening to find that there is no evidence of carcinogenicity from these devices. As Dr. Taylor cogently explained, adenocarcinoma of the corpus occurs primarily in the menopausal woman, to whom contraception is unnecessary. Furthermore there is no evidence that carcinoma of the body of the uterus comes from irritation; it stems rather from endocrine dysfunction.

The extraordinary papers throughout the day on mechanism were particularly fascinating. Certainly Dr. Mastroianni does not need my congratulations to make him realize the tremendous contribution he is making to this topic.

The discussion of the side effects during the course of the second day is of great importance to the physician, and I am very pleased that Dr. Pincus emphasized the point that we must separate the organic side effects from the psychogenic side effects.

Before I conclude I should like to remind you that we are not the only group to think about the difference between the prevention of conception and the production of abortion. It was called to my attention that the British Council of Churches, in their pamphlet on human reproduction which was issued in 1962, made a statement that may give a degree of solace to those of us who are concerned about theological attitudes. They said: "Our conclusion was that a distinction must be drawn between biological life and human life, and that in the absence of more precise knowledge, nidation may most conveniently be assumed to be the point at which the former becomes the latter. We agreed that abortion as a means of family limitation is to be condemned. But a woman cannot abort until the fertilized egg cell has nidated and thus becomes attached to her body...we see no objection...to the use of a technique which would prevent implantation. Such a method, which might be described as contra-nidation, could also quite properly be called contraception."*

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* *Human Reproduction: a study of some emergent problems and questions in the light of the Christian faith*, 44-45. British Council of Churches. London, 1962.

Obviously there are eminent theologians on our side even if it is proved that fertilization is not prevented by the IUCD. I share Dr. Mastroianni's hope—perhaps his belief— that the IUCD prevent fertilization, but even if that should not be the case, if fertilization is achieved, it doesn't necessarily mean that the whole battle is lost and that we are producing abortion

One may conclude from the two days spent here that the IUCD technique has spread with extraordinary rapidity, as indicated by the avidity with which patients accept it. I have been told by several people who visited Hong Kong recently that women actually queue up to be fitted with these contraceptive devices. One cannot challenge the fact that acceptance of it by the very people who need birth control the most is extraordinarily high. We have heard about the "cafeteria" method and that when a large choice of methods is offered, more than 50 percent and usually 80 percent of these patients choose the IUCD.

One can say without contradiction that this technique has extraordinary effectiveness in preventing conception.

I think we also should say —and this statement is made especially for those who are not physicians—that even though we have discussed in great detail the relative difficulties, the side effects—the undesired results that occur in a certain percentage of cases—have not been dangerous; they have not threatened life. As far as I know, not one of the 100,000 women or more in the world now using modern devices has died therefrom. To be sure, there are side effects, and they cannot be ignored. Nevertheless, I think we have to put them into proper perspective.

One thing that we must remember, particularly those who are not physicians, is that we must create a kind of value equation. We have to equate with the side effects and with the potential dangers, even though minor, which one faces with both intra-uterine devices and oral contraceptives, the dangers which would occur to the woman if these methods were not used and she became pregnant. Maternal mortality is very high in many parts of the world. Having a child is not without danger. Furthermore, some of the women who became impregnated would undoubtedly seek abortion, and when you add the potential danger of a pregnancy carried to term, and the potential danger of an abortion in that group of women who would seek it, their sum is far greater than the slight potential danger from either the use of orals or IUCD.

People unqualified in this field are prone to say: "Use another method, and avoid all potential danger." They say: "My God! Why doesn't that man use a condom or the woman a diaphragm or some other vaginal method?" They fail to realize that the women who use the IUCD or the pills most avidly will not use any other contraceptive method.

I leave this meeting with a great sense of optimism. I leave it with a feeling that we can now talk about controlling a population, whether it is through the use of IUCD or orals. I must point out again that much has been accomplished in two short years. When we observe the progress of the two years behind us, and look forward to the certain progress of the next two years ahead, we can be sure that the IUCD of today will be greatly improved by the IUCD of tomorrow.

APPENDIX

ADDITIONAL PAPERS AND ABSTRACTS OF WORK NOT PRESENTED AT THE CONFERENCE

General — Clinical Programs — Special Clinical
Problems — Pathology — Design of Intra-Uterine
Contraceptive Devices — Mechanism of Contraceptive Action

General

Population program in Chile

G. Adriasola and O. Avendano, *University of Chile School of Public Health and Medical School, Santiago, Chile*

There is a significant increase in interest in population problems among Chilean leaders. An annual population growth of 2.5 percent seriously counteracts economic development. Birth rates ranging around 3.5 percent are aggravated by the migration of people from rural areas to overcrowded cities. Maternal mortality is still very high—33.3 per thousand live births—and it is due to abortions in nearly 40 percent of the total cases.

Over 130,000 abortions occur annually, as compared to 290,000 live births. At least two thirds of these abortions are known to be illegal or criminally induced. This means that the Chileans are approaching their population problems the wrong way.

The Comite Chileno de Proteccion de la Familia, backed by The Population Council, convened the health authorities and the medical profession of the country and succeeded in its aim to get a clear-cut recognition of the problem and of the responsibilities lying on them. The Comite has done much to collect the necessary data and to standardize the research methods, in a cooperative effort to plan for future action.

Six professional groups of the University of Chile and the National Health Services are carrying out a comprehensive study of the use of intra-uterine devices and other contraceptives among the lower socio-economic levels of the metropolitan population.

Four of the seven clinics in this study began operations only this year—the most recent one in September. To date approximately 6,700 IUCD have been inserted, and about 500 patients are using other methods. Follow-up records have not yet been completely tabulated, but the preliminary reports are very promising. We have come to the conclusion the IUCD will actually prevent many abortions and will be much more acceptable than other contraceptive procedures.

What will be the effect upon family and community life of the extensive and successful practice of contraception? This question was raised in Chile at a conference about a year ago, and we are now drafting a research program intended to define and control the social changes that may be expected. We hope to have a unique opportunity to study the population dynamics associated with relatively sudden introduction of family planning practices.

The use of intra-uterine contraceptives by 72 general practitioners in 32 countries

Clarence J. Gamble and David Burleson, *The Pathfinder Fund, Milton, Massachusetts*

The usefulness of intra-uterine contraceptive devices in the countries where widespread contraception is needed depends upon whether the average medical practitioner, and not only Obs-Gyn specialists, can safely employ them. The Pathfinder Fund instituted a study of this question by furnishing supplies of devices and inserters to qualified physicians who agreed to cooperate. Few of the physicians had personal instruction in the technique of insertion, but depended upon the printed directions furnished by the originators of the devices used (Lippes loops and Margulies coils). Record forms were provided, which the physicians forwarded periodically to the Pathfinder Fund for analysis. The first shipment of supplies was made to Korea in August 1962; the program in other countries began in May 1963.

Reports have been received from 72 physicians in 32 countries in Africa, Asia, Europe, Central and South America. The series included 3,996 women, of whom 2,630 were examined subsequently. Of those re-examined, 11.1 percent had expelled the device. Only 3.8 percent were exposed to pregnancy by expulsions they did not notice. The device was removed from 9.4 percent of those re-examined, chiefly because of bleeding. Pelvic infections, none of them serious or of long duration, were recorded for 25, or 1.0 percent. Pregnancies were reported by 18, or 0.7 percent. These preliminary results indicate that the use of general practitioners is feasible.

Population increase and control in Turkey

Necdet Erenus, *Medical Consultant on Family Planning to the Ministry of Health and Social Assistance, Government of Turkey*

The adverse economic and social effects of rapid population growth, and the widespread resort to illegal abortion as a method of family limitation, led to the incorporation of family planning in the Turkish Five Year Plan of 1963. Various actions have been taken preparatory to launching a full-scale national family planning program. A small program was undertaken to establish the feasibility of intra-uterine contraception and to gather data with which to counter the view occasionally voiced that insertion of a foreign body might cause infection or cancer. In this program, 134 patients were given spirals, loops, or bows between June 1963 and July 1964. Detailed follow-up of each case was not attempted. Two pregnancies, 11 removals, and three expulsions were recorded. Removals were due principally to prolonged or excessive bleeding. It is noteworthy that a distinct difference in reaction was observed between the literate, high-income patients and the poor, illiterate patients. The former were almost the only ones to develop pain or bleeding to any appreciable extent; the illiterate groups were almost unanimous in their satisfaction with IUCD. It is anticipated that intra-uterine contraception will play a substantial part in future family planning developments in Turkey.

Clinical Programs

An evaluation of the intra-uterine contraceptive device in a group of 50 women

W.A. BONNEY, Jr. and Charles COOPER, *Dept. of Obstetrics and Gynecology, Vanderbilt University School of Medicine, Nashville, Tennessee*

Fifty parous women have used a Margulies 5-J intra-uterine contraceptive device for a period ranging from eight weeks to fifteen months. The study evaluates the following factors: (1) contraceptive effectiveness, (2) undesirable side effects, (3) histology of endometrial biopsies taken prior to insertion, compared with eight or more weeks following insertion, (4) histology and biochemical studies of the endometrium in certain cases following vaginal hysterectomy and unilateral salpingectomy, and (5) recovery of spermatozoa and ova from the fallopian tubes in certain cases following extirpation at particular times in the menstrual cycle.

Contraceptive effectiveness: No pregnancies have occurred in this group of 50 patients with a total exposure period of approximately 15 woman-years. Two patients did become pregnant within two months after the removal of the ring. *Side effects*: Seventy-eight percent of the patients noted some degree of metrorrhagia, 40 percent some menorrhagia, 58 percent cramping, 40 percent noted some discharge, 8 percent developed a clinical pelvic infection necessitating the removal of the contraceptive coil for a period of one to two weeks. Ten percent were dissatisfied with this contraceptive method and wished to change to other birth control measures. Thirty percent of the patients lost the contraceptive coil during the study period; each of these patients realized that the ring had been lost and promptly returned to the clinic for reinsertion. All of the undesirable side effects other than the loss of the contraceptive coil occurred in the first eight weeks after insertion. *Histology of endometrium and fallopian tubes*: Evaluation of the histological sections showed a very low incidence of acute endometritis. The fallopian tubes in ten cases which required surgery for pelvic relaxation were normal. *Tubal content studies*: Ova were recovered from the fallopian tubes in two patients. One of these ova was fertilized, showing two pronuclei. At least in this one case, the coil did not prevent fertilization of the ovum. The other recovered ovum was not fertilized.

Report on the use of intra-uterine devices in Hong Kong

S.Y. CHENG, Y.L. WONG, and D. CHUN, *Hong Kong Family Planning Association*

This report covers a series of 4,048 patients observed from June 1963 to August 1964, with a total exposure of 15,822 woman-months. The devices used were Margulies spirals (376) and Lippes loops (3,672). The average age of the users was 32.6 years, with a range of 20 to 48 years. The average number of living children was 4, with a range of 1 to 14. The average income per family per month was HK $309.

Two hundred and sixty (6.4 percent) women requested removal of the device; the chief reasons given were bleeding, abdominal pain, and lack of confidence. Sixty-two (1.6 percent) women abandoned this method because of repeated expulsions and 36 (0.9 percent) because of accidental pregnancies. The remaining 3,690 (91.1 percent) women tolerated the device well and were completely unconscious of its presence.

Of the 36 cases of accidental pregnancies, the device was removed from 22, found displaced in the vagina in 2, and not found in 12. There was no ectopic pregnancy.

There was a total of 433 expulsions, or 10.6 percent of all insertions; 20.4 percent of the Margulies spirals and 9.6 percent of the Lippes loops were expelled. With the exception of 62 cases who preferred other methods, the rest (371) requested reinsertions (maximum 4 times).

In our experience in Hong Kong the use of intra-uterine devices has given us very satisfactory results, with an accidental pregnancy rate of only 0.9 percent. It is acceptable to a high percentage of users; at the end of the period of observation the number of women still using this method was 3,690 (91.1 percent). It was also found free of serious complications such as hemorrhage and pelvic inflammatory diseases.

Effectiveness and acceptability of intra-uterine devices

H.W. HORNE, Jr., C.G. CASEY, H. NAFICY, and P.G. BROOKS, *Boston Lying-in Hospital, Boston, Massachusetts*

In our series, 110 patients have had insertions of intra-uterine contraceptive devices since December 1962. There have been two pregnancies, both within a few months of insertion, and both using small devices which are no longer being utilized. One of these had the device removed at six weeks gestation, and the other ejected the device at 38 weeks. Both delivered normal, full-term infants. There have been twelve patients (10.9 percent) who ejected the device, five of whom have been able to wear a different device or size without complications. Nine patients (8.2 percent) have required or requested removal of the device because of excessive or annoying bleeding. There has been no significant trauma resulting from insertion or wearing of such a device, and we have had no pelvic infection caused or reactivated by an IUCD.

Fourteen months' experience with the intra-uterine contraceptive device

Ann H. HUIZENGA and James F. DONNELLY, *North Carolina State Board of Health*

To ascertain the acceptability of the intra-uterine device by a rural population of low socioeconomic status, the North Carolina State Board of Health initiated a trial of the Margulies spiral in eight rural counties.

Admission to the study was voluntary and with full understanding that the device was being used on an investigational basis. Patients were assured that the device would be removed at any time on request.

Five hundred and forty-four women (124 white, 354 Negro, 66 Indian), married and presumably living with their husbands (with three exceptions), comprise the basis of this preliminary report. Parity ranged from one to over 20; age from 15 to 44 years. One hundred and seventy-nine had completed some grade school, 318 some high school, 16 some college, and two some graduate training; the education of 29 is unknown. Four hundred and fifty-one (83.0 percent) have the device in place. Of the remaining 93, four have had tubal ligations, nine have had hysterectomies for gynecological reasons, six have moved away following expulsion or removal, eight transferred to other states, and five have been lost to follow-up.

Of the remaining 61 (11.2 percent) temporarily closed, reasons for discontinuance include:

Bleeding and/or cramps or pain	18
Husband's objection	12
Fear and lack of confidence	10
Pregnancy after expulsion or removal	6
Awaiting reinsertion	5
Pelvic inflammatory disease (or infection)	4
Unfavorable publicity	4
Investigator's decision	2

These 544 women have accumulated 2,379 woman-months of exposure. No pregnancies have been known to occur following insertion with the device in place. Five women developed pelvic inflammatory disease; three required hospitalization. All responded readily to antibiotic treatment.

General acceptance has been most gratifying amongst public health personnel and patients. Acceptance by local physicians, however, has ranged from interest to distrust and even objection.

Long-term use of various types of intra-uterine contraceptive devices in women of high fertility

Margaret C.N. JACKSON, *Medical Officer to Devon Clinics, I.P.P.F., Crediton, England*

Silver Gräfenberg rings were first used at the Exeter Clinic in 1939, and their use was continued until 1962, when the Lippes loop No. 1 became available. Thereafter new cases were fitted with the Lippes device, and old cases who came for check-ups had their metal rings exchanged for the new plastic devices. There was at first some resistance to the change, both from patients and their doctors. There were eight pregnancies with the small Lippes loop soon after they were substituted for Gräfenberg rings. Subsequently, a larger choice of plastic devices became available, including larger loops and the Birnberg bow, and results have steadily improved.

In all, 196 patients were fitted with a Gräfenberg ring; 86 of these cases were closed, and 110 were changed to a plastic device. New cases fitted with plastic devices total 324. Experience with plastic devices totals some 5,000 woman-months. Some reduction has been noted in the number of cases requiring removal of the device because of menorrhagia, pain, or discharge. The number of expulsions is about the same as for Gräfenberg rings. There have been no expulsions or pregnancies among the 50 cases who have so far been fitted with small Birnberg bows. The fear of coming to be fitted or have the device changed has completely vanished since the advent of plastic devices has removed the need for dilatation of the cervix.

Evaluation of intra-uterine devices in Jamaica

LENWORTH JACOBS, *The Beth Jacobs Clinic, St. Ann's Bay, Jamaica, West Indies*

During the first year of study, 371 devices have been inserted, equally divided between Margulies spirals and Lippes loops. More than 90 percent of cases with initial insertions have continued to use the method. The major reason for discontinuations has been involuntary extrusion. In this series, 20 patients experienced this event. The insertions have been done irrespective of the presence of cervicitis, a common condition in our population. Cervicitis was diagnosed in 304 patients at the time of insertion, 37 had trichomonas, and 31 had gonococcus. Papanicolaou smears were taken on all patients at the time of insertion and are repeated regularly.

Interim summary of work in Fiji with intra-uterine devices

E.E. Knowles, *Family Planning Clinic, Colonial War Memorial Hospital, Medical Department, Suva, Fiji*

The study of intra-uterine devices in Fiji, using the Lippes loop, began in January 1964. During the first month, only 13 loops were fitted. However, from February to the end of July 370 cases were studied. In the first few weeks of the study, patients were brought back for follow-up very frequently, i.e., at weekly, bi-weekly, monthly, then bi-monthly intervals. At present we recall patients one month after insertion and then semi-annually, unless there are complicating factors. Of course, any case is free to visit us at any time between appointments should she wish to do so. An explanatory leaflet has been prepared about the loop with simple instructions in English, Fijian and Hindustani. Of the 370 cases collected up to July 30, practically all are Indians, with a small number of Fijians, part-Europeans, and Europeans. Most of the women are in their late 20's or early 30's and the majority are multiparas with four or five children. Most of them have either used no contraceptive before or have been on oral contraception. There were six failures to insert due to a variety of reasons (e.g., scarred cervix, intra-uterine fibroids) but of these, three were inserted successfully on a second attempt. Eight cases expelled the device, and six of these were reinserted and have since retained the loop. Two cases had fairly severe pain following the insertion but responded to treatment. Five cases were treated successfully for cramps. Ten cases with either spotting, heavy periods, or intermenstrual bleeding were treated and controlled. Seven loops have been removed after insertion. One case had misled us regarding her periods and an early pregnancy existed when the loop was inserted. The husband of one case insisted on removal as he considered that his wife "could not be trusted if she had the protection of a loop." Five cases had prolonged spotting, intermenstrual bleeding or menorrhagia which did not respond to treatment. The method is considered safe and easy for relatively uneducated and unmotivated people. This is now the method of choice offered first to all our new patients in Suva, and we hope to extend the use of the IUCD to other centres in Fiji in the near future.

Current experience with an intra-uterine contraceptive device

W.H. Kreienberg, *The Planned Parenthood League of Rochester and Monroe County, Rochester, New York*

Intra-uterine devices of the Lippes type were inserted in 1,111 patients. This is equivalent to 7,428 woman-months of use. Complications, including extrusion, pregnancy, bleeding, cramps, and miscellaneous have involved a total of 178 patients. This is a complication rate of 16 percent. Total pregnancies to date have been 10, of which three have occurred with the device in place, five with the device undetermined, and two with the pregnancy occurring prior to the insertion of the device. This gives an uncorrected pregnancy rate of 1.61 per 100 woman-years of use.

Experience with Birnberg's intra-uterine device in Kuala Lumpur: preliminary report

S. LOURDENADIN, *Dept. of Obstetrics and Gynecology, Maternity Hospital, Kuala Lumpur, Malaysia*

A few statistics will furnish the background of family planning activities in Malaysia. A population of nearly 8,000,000 inhabits an area of 50,000 square miles. In 1961 the birth rate was 41.9 per thousand population and the crude death rate 9.2 per thousand. Maternal mortality was 2.4 per thousand total births, and infant mortality 60 per thousand live births. The rate of population increase was 33 per thousand.

The administration is neutral towards family planning but gives a grant from welfare funds and allows family planning workers the use of the maternal and welfare clinics. The general assumption is that the country can support twice the population. However, with the present five-year plan for industrialization and efforts to improve the rural economy and raise the standard of health and living, the idea of family planning is being given more heed than hitherto, and eventually we visualize the pre-pregnancy health measures will form part of the over-all care of mothers in the health clinics.

Until recently the conventional methods of contraception have been in use and during the last five years oral contraception has been the method of choice. The orals are not wholly satisfactory, mainly because of the regimen necessary for their use, and partly because of side effects. Intra-uterine contraceptive devices come closer to the ideal method: they are simple, effective, within the means of the poorest, aesthetically acceptable, and the evidence obtained so far shows them to be harmless to both husband and wife and to the future children.

Intra-uterine contraceptives were first introduced in Malaya early in 1964, when a study was begun at the postnatal clinic of the Maternity Hospital in Kuala Lumpur. The Birnberg bow (16 mm wide) is being used in this study.

Preliminary examination excludes patients with obvious pathological conditions (fibroids, ovarian cysts, acute and sub-acute pelvic inflammatory disease, etc.); cases of infected cervical erosion are treated by electrocautery six weeks before insertion. Patients with irregular menstrual cycles, who are better managed with the oral contraceptives, are also excluded. The bows are inserted either six to seven days postpartum, or about the seventh day of the menstrual cycle—although this is often not possible with patients reluctant to make a second visit to the clinic on the appropriate day. The bows are sterilized by keeping them in 1 : 1000 Zephiran solution, the inserters by boiling. Pap smears are taken routinely at the time of insertion and every six months thereafter.

The aim is to follow about 500 patients for a year and if found satisfactory to introduce the method in other centers in the country. Detailed records of expulsions, removals, and pregnancies will be kept. It is intended also in this pilot study to collaborate with workers in the Institute for Medical Research in conducting bacteriological studies of the uterine cavity for these cases, and to do histopathological studies of the endometrium as well as the uterus after hysterectomy, especially in the older groups, following varying periods of insertion.

The acceptability of the method to both wives and husbands appears high. A total of 150 cases have been fitted with Birnberg's bows during the last seven months, 67 percent of them in postnatal cases about six to seven weeks after delivery. Their average age is 32, average parity 6.2. In 10 percent there were mild complications such as menorrhagia, leukorrhea, and lower abdominal discomfort, which subsided with encouragement and reassurance. In one case the IUCD was removed because of menorrhagia, possibly due to early insertion, i.e., four weeks after delivery. During the short period of trial totalling 543 woman-months, Birnberg's bows have proven to be a safe contraceptive with minimal side effects that subside with time and reassurance. No pregnancies have occurred, but more extensive use over a longer period is necessary to give a true picture of their contraceptive effectiveness.

Clinical use of the nylon coil in Ipoh, Malaysia

ARIFFIN BIN NGAH MARZUKI, *State Gynecologist, General Hospital, Ipoh, Perak, Malaysia*

During a year's trial period, June 1963 to June 1964, 264 patients were fitted with coils made of nylon, using a metal inserter. The instruments are sterilized by boiling. Sixteen patients had the device removed; 54 had spontaneous expulsions. Two pregnancies were recorded, giving a pregnancy rate of 1.3 per 100 woman-years. By mid-September 1964, 300 patients were wearing the device and were being followed up regularly. The method is easily performed in the clinic of the Ipoh General Hospital, and may be the best method to adopt in Malaysia.

Experience with intra-uterine contraceptive devices

Warner NASH, *Department of Obstetrics and Gynecology, Lenox Hill Hospital, New York City*

Three and a half years' experience with polyethylene and stainless steel devices in 300 patients for 5,680 woman-months of use resulted in an over-all failure rate of 2 percent.

However, four pregnancies occurred in patients who lost a device without their noticing it during the early phase of this study; only one pregnancy occurred with the device *in situ*, and one with no knowledge as to location. No pregnancies were noted with the Lippes loop in 170 patients. For various reasons, 3.2 percent of the patients discontinued the method. There were four removals for desired pregnancy, all followed promptly by conception. There was one removal because of cramps, and seven for staining or bleeding; endometrial biopsies in these showed normal appearance in six, and a decidua-like endometrial lining in one patient.

A careful encouragement of trust and understanding with each patient was felt to be a significant factor contributing to the effectiveness of the method. This helped to alleviate psychological concern about the method, as well as minor symptoms accompanying initial reactions to its use. Careful instruction, detailed explanation, and good follow-up were used to promote this attitude.

This method was found safe as well as effective, well liked, and in general well tolerated by patients and their spouses. Subsequent fertility was not impaired and no abnormal cytological smears were found.

Experience with plastic intra-uterine contraceptive devices (Lippes loops) in Egypt

M. KAMAL ABDEL RAZZAK, *Director General, Egyptian Association for Population Studies, Cairo*

Encouraged by the reports presented at the first conference on intra-uterine contraception in 1962, we have initiated a study on the use of the Lippes loop in clinics in Cairo and Alexandria. Supply problems delayed the study; it has been in progress two months, and 106 loops have been inserted. There were four spontaneous expulsions, two were removed for bleeding, and one because of pain.

It is apparent that the polyethylene loop does not solve the problem of spontaneous expulsion, which has also been troublesome in 30 years' experience with devices made of silkworm gut.[1] On the other hand, there are no expulsions to report for another device—a stainless steel ring, obtained from Bell and Croydon, London. These are much stiffer than silkworm gut or polyethylene. It is suggested that resilience facilitates expulsion, and that a less resilient plastic device might help solve this problem.

1. Razzak, M.K.A.: "Intra-uterine contraceptive devices", *Intra-uterine Contraceptive Devices* (C. Tietze, S. Lewit, eds.), 53-56. Amsterdam: Excerpta Medica International Congress Series No. 54, 1962.

An evaluation of intra-uterine contraceptive devices

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This is a study, conducted by the Albert Einstein College of Medicine, of the effectiveness and safety of two intra-uterine devices (the Lippes loop and the Birnberg bow), and an attempt to evaluate the acceptability of each device to a low-income, semi-indigent, urban, largely Spanish-speaking population group. The study is being conducted at two municipal hospitals in New York City, the Jacobi and Lincoln Hospitals.

During the past year, an unselected group of more than 600 women have been fitted with the devices. Approximately 60 percent of this group are Puerto Rican in origin; approximately 30 percent are Negro Americans; and approximately 10 percent are white Americans. The group is to be observed for a five-year period. During the first year there will be three checkups of each patient, and thereafter there will be semi-annual checkups. Papanicolaou smears and endometrial biopsies are to be done at all visits.

The study began in September, 1963. As of October 1, 1964, there were 664 patients in the study group. The Lippes loop had been inserted in 347 patients; Birnberg bows of various sizes had been inserted in 311 patients; and Margulies coils had been inserted in six patients. Eight patients had been using the device nine months; 57 patients six months or longer; 284 patients four months or longer; and the remaining 315 patients for periods of less than four months.

As of August 1, 1964, the devices had been removed in 37 cases (approximately 5 percent of the group) at the request of the patients; the primary reasons advanced for requesting removal were pain and excessive bleeding. Expulsion of the device had occurred in 27 of the cases (approximately 4 percent of the group); 16 of these expulsions were noticed by the patients and 11 were unnoticed.

As of August 1, 1964, there had been 13 pregnancies in the group (approximately 2 percent of the corrected total of the group). All of these pregnancies occurred with the devices in place: nine with the Birnberg No. 3, one with the Birnberg No. 5, and three with the Lippes No. 2.

As of August 1, 1964, the following complications had been noted in a few of the cases: severe pelvic inflammation (one case); device embedded in myometrium (same one case); severe metrorrhagia (seven cases); severe pain and syncope after insertion (seven cases); removal requiring dilatation and curettage (three cases).

Summary of experience with intra-uterine contraceptive devices

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From December 15, 1963 to August 15, 1964, intra-uterine devices (Lippes loop No. 2) were inserted in 165 patients, most of them during the past three to four months. Prior to insertion, gynecological examination, including Papanicolaou smear, was carried out. In one case a lesion was detected; this patient was not included in the data. Our trials have been restricted and characterized by caution and reserve, because until recently intra-uterine contraceptive devices have not been used on a large scale in Denmark, and the medical profession on the whole has been hesitant about accepting this contraceptive method. The main indications for prescribing intra-uterine contraception have been: (1) repeated failures with the diaphragm method — a large group of our patients have had one, two, or three induced abortions, which are legal according to the Danish Pregnancy Act, (2) as an alternative for sterilization, for women whose application to be sterilized was denied by the Ministry of Justice, (3) mental incapacity to use correctly any other kind of contraception, (4) hypersensitivity to rubber, spermicidal foams, etc.

The expulsion rate has been four out of 165 patients. In eight cases the loop was removed due to continuous and lasting metrorrhagia beyond the first month, in two cases due to constant pain in the lower abdomen. In two cases acute salpingitis occurred, but after treatment with antibiotics the symptoms disappeared and the loop was left *in situ*. During the time of observation no pregnancy occurred.

Clinical experience with three intra-uterine contraceptive devices

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Over two and a half years' experience in the use of three types of intra-uterine device at the Margaret Sanger Research Bureau has been assembled. The Margulies spiral size 5, the first device, was inserted in 286 women during 1962 and 1963; from August 1963 to March 1964 the Birnberg bow size 3 was used in 210 women; the Lippes loop size 3 is the device currently being evaluated. In the first seven months of 1964, 171 loop insertions were made. The follow-up data, brought up to date as of June 30, 1964, include relevant and non-relevant reasons for removal, number of spontaneous ejections, failure (unintended pregnancy) rates, and the Papanicolaou findings through July 31, 1964. The last show no significant changes for periods of use of 28 months for the spiral, 10 months for the bow, and three months for the size 3 loop.

Experience with intra-uterine contraceptive devices

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For this study patients were mainly selected who had been admitted to the hospital for legal interruption of pregnancy or for "spontaneous" abortion in unwanted pregnancies. In all patients the conventional contraceptive methods had either failed or had not been used, due to aversion or lack of intelligence. The data includes only women with proven fertility and constant exposure to conception. Lippes loop size 2 was used in the majority of cases, and the Margulies spiral was used occasionally. About 90 patients have been treated so far; the majority within the last six months. No pregnancies have occurred. In six cases the device had to be removed because of bleeding or pain, but it was our impression that emotionally unstable patients exaggerated their symptoms. In one case, a Lippes loop was expelled, but the Margulies spiral that was inserted in its stead remained in place. Bleeding is frequent and often rather strong during the first cycle and the first menstruation is often stronger and more prolonged than usual. After the first month the symptoms are usually negligible. The great majority of the patients are satisfied with the method, which greatly improves their marital relations. The sutures in the Lippes loops are often invisible at control examinations, and it is our belief that they are unnecessary. In cases of doubt, the loops are easily visualized by X ray. In one instance a myometrial strip was removed at laparotomy from a uterus with a Lippes loop in the cavity. The motility pattern and the oxytocin sensitivity showed no striking differences from that of strips removed from normal uteri at the same stage of the menstrual cycle.

The Birnberg bow as an intra-uterine contraceptive

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A study was begun in June 1964 which proposes to increase our knowledge of the influence of the Birnberg bow on conception, genital bacterial flora, and the endometrium in a carefully selected group of 200 clinic patients. A No. 5 Birnberg bow is used. The patients are Protestant women, para III or greater, with medical or personal need for contraception. Cervical and intra-uterine cultures are taken before insertion of the bow, and will be repeated at three and six months. Endometrial biopsies will be taken six months after insertion of the bow.

To date 31 patients have been entered in the study. Two have complained of cramping, two of irregular bleeding. There have been no expulsions or pregnancies. Acceptance of this method of contraception by the patients has been uniformly eager.

A study of intra-uterine contraception in Los Angeles clinics

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This study has been in progress for about a year and a half, primarily at the main clinic of the Planned Parenthood Centers of Los Angeles, and also at the Venice Branch and The Tyler Clinic. About 400 devices, mostly inserted by the same physician, have been used, including the Margulies spiral, Lippes loop, and Birnberg bow. At the main clinic 340 patients received one of the three devices; 64 of these cases were permanently closed. The Margulies device (No. 5) was used in 176 patients; 11 of these were spontaneously expelled, with two patients requesting reinsertion. Seventeen spirals were removed because of excessive bleeding, and the remainder for miscellaneous reasons, including lack of confidence, pelvic inflammatory disease, and husbands' complaints. No pregnancies occurred in those cases retaining the spiral. The Lippes loop (No. 2) was inserted in 81 patients and there were seven spontaneous expulsions, with five reinsertions. One pregnancy occurred among Lippes loop patients. Among 83 patients with the small or large Birnberg bow there were two spontaneous expulsions, three removals because of excess bleeding, and five removals for miscellaneous reasons. Five pregnancies occurred among Birnberg bow patients, four with the small size of bow. There were only two serious bleeding complications in this series, one patient requiring removal of the device and emergency transfusion, and the other removal and dilatation and curettage.

Endometrial biopsies are being taken on patients when devices have been *in situ* for about a year, and salpingo-cinegraphy is being employed in an attempt to obtain data on tubal activity. Papanicolaou smears are taken at half-year intervals. On the basis of our limited experience thus far, we tend to favor the use of the Lippes loop over the other two devices. As an auxiliary portion of our study we are looking into the possibility of reducing the incidence of excessive bleeding by employing a bioflavonoid high-dosage Vitamin C preparation in a randomized doubleblind placebo study. Results of this will not be known until large enough groups on each batch are available to warrant breaking the codes. We also have the impression that patients in the private clinic series (not included in this study) seem to have somewhat lower percentages of complications than those noted above, particularly regarding requests for removals.

Intra-uterine contraception in Southern Rhodesia

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The following is a summary of our study of intra-uterine contraception through August 18, 1964. Three hundred and twelve women were fitted with an IUCD (20 with Margulies coil, nine with Lippes loop—30 mm, and the remainder with the smaller Lippes loop—27 mm). The patients had an average parity of five prior to insertion. Forty women expelled the device. Of these, 27 were reinserted once, two twice, and one three times. Nine patients expelled the device one or more times and were not interested in reinsertion. Twenty women had the device removed, 18 because of relevant reasons. A total of 25 cases have been closed. One patient wearing a Margulies coil has had no menstrual period, except for six days immediately after insertion, since June 11, 1963. She has lost considerable weight and has been referred to a gynecologist. No report on her condition has yet been received. Thirty women reported severe pain, and 27 complained of moderate pain. The conclusion reached to date is that this is an acceptable form of contraception in developing communities, and that interest among members of this community is increasing and is extending to the lower classes.

Special Clinical Problems

Results of early puerperal insertion of intra-uterine bows

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Sixteen patients were fitted with intra-uterine bows at or shortly after delivery or early abortion. No abnormal bleeding, febrility, or inflammatory sequelae were noted. In seven patients the device was inserted from the second to fourth postpartum day using an introducer. Two devices were expelled within three days. Two devices were found protruding from the cervix at the sixth week examination. One of the devices that was expelled three days after insertion was immediately reinserted. A hysterogram taken ten weeks postpartum showed one device to be in the isthmus and cervical canal. It was removed and replaced. One patient was found by hysterography at the sixth week examination to have had a downward migration of the device and it was replaced. One device was found to be *in situ* and one patient has not been seen though the device has not been expelled.

Three devices were inserted into the fundus immediately following delivery of the placenta. None was expelled. One was checked by hysterography after three months and found to be *in situ*. Four devices were inserted following early abortion, immediately after either curettage or spontaneous abortion. All of these devices were retained. One has been checked by hysterography and found to be *in situ*. One was inserted following low-flap cesarean section. The postoperative course was complicated by severe back pain but this gradually abated, and the device was not expelled.

Increasing the size of the nulliparous uterus for insertion of a contraceptive device

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In order to facilitate introduction of contraceptive devices the uterine cavity and cervical canal dimensions may be increased by the use of estrogen and progestin. Not infrequently in the nullipara the uterine cavity is small and the cervical canal at the internal os measures 2-3 mm in diameter. A uterine sound, with difficulty, may be introduced to 5 or 6 centimeters. The introduction of an intra-uterine contraceptive device is associated frequently with considerable pain, uterine cramps, and syncope. By the oral administration of estrogen and progestin for a period of two months, the size of the uterine cavity may be doubled and the cervical canal similarly will be enlarged. Although the estrogens themselves will stimulate growth of the uterus, the combination with progestin will reduce breakthrough bleeding. Premarin in doses of 2.5 mg (or estinyl 0.10) and norlutate to 5 mg (or provera 10 mg) are given for one week. The dose of each is doubled, tripled, or possibly quadrupled and continued for seven more weeks. After this therapy of eight weeks, the intra-uterine device may be inserted with little difficulty. The uterine cavity is now twice normal size. The cervical canal is soft and slightly dilated. The drugs are continued for one week following the introduction of the contraceptive device and then withdrawn. Bleeding for a period of ten days to two weeks will follow. This bleeding is usually not excessive and may be controlled by the use of ergotrate compounds.

Control of intermenstrual bleeding after IUCD insertion

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One of the most frequent side effects reported by patients following the insertion of an IUCD is intermenstrual bleeding. This disturbing complaint, which often prompts a request for removal, may be alleviated by the administration of citrus bioflavonoids, which have been reported to have anti-inflammatory properties, or ascorbic acid, which tends to increase capillary strength. Two hundred and thirty-four women were fitted at the conclusion of a menstrual period with an IUCD (Hall ring, Lippes loop, or Margulies spiral). They were divided into three groups. Group I, the controls, received no treatment. Group II took 200 mg of ascorbic acid three times a day. Group III took a capsule containing 200 mg of ascorbic acid and 200 mg citrus bioflavonoid compound. The capsules, which were identical in appearance, were labeled A and B and their contents were not identified until the conclusion of the entire study. The medication was begun on the day of IUCD insertion and discontinued after 33 days. Data on vaginal bleeding and menstrual flow were obtained from the time of insertion to the conclusion of the second menstrual period. The incidence of normal menstrual flow was virtually the same in treated and untreated groups. Normal menstruation was reported by 32 percent of the controls in the first cycle and by 62 percent in the second. The only difference between treated and control patients in regard to menstrual flow was an increased incidence of heavy menstruation among the treated patients during the first cycle. This large difference was not seen in the second cycle. Although the incidence of any intermenstrual bleeding was essentially the same in all groups in the first cycle, the treated patients showed a decrease during the second cycle. The treated patients also had a decreased incidence of heavy spotting during both cycles. Our study would seem to show that large doses of vitamin C alone are sufficient to cause a marked decrease in the incidence and amount of intermenstrual bleeding following the insertion of an IUCD.

Bleeding patterns and their treatment in women fitted with coils

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During the past four years, a total of 3,000 women have been fitted with intra-uterine contraceptive devices at Mount Sinai Hospital. The following patterns have been observed: (a) FIRST MENSES: Fifteen percent of all patients exhibited excessive bleeding for several hours. However, 85 percent of the women showed normal or moderately increased flow. The excessive bleeding may be attributed to *myometrial insufficiency*, a failure to adapt to the foreign body. In almost all cases, control of this condition was achieved with ice-bags, *Methergine* or *Ergotrate* (2 tablets every 30 minutes, maximum 8; or 2 injections 30 minutes apart). (b) LATER DISTURBANCES: Eighteen percent of the patients show intermenstrual spotting and bleeding (besides *Mittelblutung*). In half of them it occurs only occasionally, but in the other half it is due to a *syndrome of general capillary fragility*. (These women gave a history of bruising easily—many have hematomata on thighs—and their gums bleed easily.) It would seem that their endometrial capillaries are bruised when uterine contractions move the device in the cavity. This general tendency for bleeding can be controlled within a few weeks with 2 gm of ascorbic acid daily. Preferably, they should continue this inexpensive medication for four months. An additional one percent of the patients suffer from *endometrial hyperplasia or inflammation*. They respond, respectively, to curettage or antibiotics. Failures of the described regime are due to pre-existing pathology such as adenomyosis, submucous fibroids, or polyps. It should be noted that some normal healthy women without IUCD *in situ* also develop these syndromes.

Pathology

Study of tissue reaction in hysterectomy specimens removed after insertion of intra-uterine contraceptive devices

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Sixty-two women from the postpartum clinic at the Bayamon Health Center, for whom hysterectomy is planned for mechanical difficulties (i.e. prolapse) have been fitted with intra-uterine contraceptive devices. Hysterectomy is performed at various intervals after insertion. Pre-insertion endometrial biopsies have been studied. Twenty-three hysterectomies have been performed; 11 with Margulies spirals No. 5 and 12 with Lippes loops No. 2. Two patients had experienced insertion with two different devices because of expulsion of the first device inserted. The time of the devices *in utero* has varied from one week to 36 weeks. Of the 16 cultures of the endometrial cavity, taken at hysterectomy by stab-wound through the posterior wall of the uterus, six grew out *S. albus* and one *B. subtilis*. The remainder showed no growth. Eight cultures were taken from controls and three grew *S. albus* and one alpha hemolytic streptococcus. Four uteri without devices have been examined histologically as controls.

Endometrial morphology, histochemistry, and biochemistry of endometrial secretions in wearers of the intra-uterine stainless steel ring

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Endometrial tissue samples are being obtained by biopsy cannula before and after insertion of the intra-uterine stainless steel ring and examined for morphological and histochemical changes. Each patient is assigned "biopsy dates" on which endometrial tissue samples are taken before insertion of the ring, after one complete cycle with the ring *in situ*, and every third month thereafter. The procedure has been planned in such a way that a sufficient number of representative specimens of each day of the secretory phase are obtained for study. Biopsies obtained prior to insertion of the ring serve as controls and permit comparison of the findings in the same patient and from the same day of the cycle. In this manner over 100 cases have been followed up for up to 15 months. In addition, nine women were fitted with the intra-uterine stainless steel ring prior to hysterectomy for the treatment of prolapse. Full thickness step serial sections of these uteri were subjected to histological and histochemical examination.

To date the results of this study have shown:

1. no evidence of inflammatory changes or foreign body reaction;
2. no evidence of infection;
3. no evidence of necrosis at points of contact;
4. no evidence of deviation from the typical cyclical changes of the endometrium;
5. no alteration in the degree of progestational change of the endometrium, indicating: a) no evidence of alteration in ovarian activity, and b) no evidence of alteration in endometrial responsiveness to the ovarian hormones;
6. no evidence of pregnancy or abortion;
7. no evidence of change in the distribution of alkaline phosphatase;
8. no change in the staining reaction with PAS;
9. an increase in the staining reaction with Alcian blue in two thirds of the specimens, indicating an increase in the depolymerization of the mucopolysaccharides in the ground substance, as compared to the pre-insertion biopsies;
10. no change in the results of cervical cytological examinations carried out at three-month intervals.

Results from the histological examination of hysterectomy specimens parallel those obtained from endometrial biopsies. Endometrial mucus specimens are being obtained by means of an intra-uterine collecting device and examined for physical, chemical, and enzymatic properties. Results of these examinations before and after insertion of the intra-uterine pessary will be compared. Only preliminary results are available at present.

Cytological and histological studies after prolonged use of intra-uterine contraceptive devices

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At the request of a town in Iwate Prefecture we recently conducted a screening test of 1,553 women for uterine cancer. It was discovered that 72 had received an intra-uterine contraceptive device (IUCD) many years previously. The main reason for opposing the use of intra-uterine devices has been that they may cause a malignant neoplasm, particularly cancer of the uterus. Cytological, colposcopical, and histological examinations on these 72 women were therefore carried out, with the following results.

All 72 were over 30 years of age, and had been wearing an IUCD for an average of 3.1 years. The distribution of cytological and histological findings in the IUCD group and non-IUCD group were compared. Of the non-IUCD group, 51 percent demonstrated Class I Papanicolaou smears, 41.9 percent Class II, 6.3 percent Class III, and 0.4 percent Class IV. In the IUCD group, 63.9 percent had Class I smears, 33.3 percent had Class II, and 3.0 percent Class III. All women with Class III or IV smears and with cervical erosion were recalled for biopsies. Up to now, six cases of uterine cancer in women wearing an IUCD have been reported in Japan; however, from the histological examination it was clear that each of these cases had no relation to the foreign body inserted into the uterine cavity. In the present study, eight cases of primary uterine cancer were discovered in the 1,481 women who had no experience with intra-uterine contraception. Among the 72 patients who had the IUCD, eight individuals had worn a device for over five years; these demonstrated Class I or Class II smears.

Effect of intra-uterine contraceptive devices on brush smears of the endometrial cavity

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During the period from December 1, 1963, through July 20, 1964, 221 women have received IUCD: 111 Birnberg bows No. 3 and 110 Lippes loops No. 2. Endometrial brush smears (Papanicolaou stain) were made before insertion of the device in 100 unselected patients of the group; 76 of these have had a second brush smear of the endometrial cavity taken after the device has been in the uterus for four months. (The remaining 24 patients have not yet attained the four-month period.) Final smears will be taken of the 100 patients when the device has been *in utero* one year. No significant smear changes have been noted to date.

Additional observations among the 221 patients include: one pregnancy (now in progress) with the Birnberg bow either *in situ* or lost without knowledge; two spontaneous expulsions of the Lippes loop—both reinserted, one retained and one expelled a second time; two cases of cervical carcinoma *in situ* (initial Papanicolaou smear confirmed by biopsy) leading to hysterectomy; and two removals for medical reasons (one dysmenorrhea and one persistent metrorrhagia).

Vaginal and cervical histology of women using plastic intra-uterine devices

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Papanicolaou smears were taken from the vaginal pool, the cervical surface, and by endocervical aspiration from 1,201 women in Puerto Rico before and at various intervals following plastic coil insertion. Anaplastic (type III) smears were observed prior to insertion in approximately 3 percent of these women. Among the women with negative smears prior to insertion, type III smears developed after a mean interval of nine months in about 3 percent. In approximately 50 percent of the women developing such anaplastic smears a reversion to a negative smear was observed after an average interval of 4.3 months, and among one sixth of these a return to grade III smears occurred in a mean interval of 6.2 months. There is a tendency toward increasing frequency of suspicious vaginal smears in longer-term users. Only one case of carcinoma *in situ* has been diagnosed in approximately 60 cervical biopsies.

Endometrial histology in women using Ota's ring

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Most Japanese and other investigators have found no distinctive changes in the endometrium of women wearing rings or loops. Is it sufficient to take a biopsy of only a small portion of the endometrium for determining the effect of intra-uterine devices on the endometrium? To answer this question, we are presently employing techniques to study three distinct sections of the uterus: 1) an area free from the ring, 2) an area loosely attached to the ring, and 3) a section firmly in contact with the ring. Endometrial biopsies were made on 73 clinically normal patients at the time of routine change of devices, by curetting the uterine mucosa. Devices are usually changed every two years. Of the devices used in our patients, 51 were made of metal and 22 of polyethylene. The following results have been noted: 1) About half of all devices were covered by a thickened endometrium. 2) Cell infiltration, fibrosis and necrotic changes were more intensive and common in the firmly attached sections than in the free areas. 3) Cyclic changes in the firmly attached sections were not different from those sections free of the device. 4) Squamous metaplasia of the endometrium was found in a few cases. 5) Light, round and enlarged cells as seen in the endometrium associated with the presence of chorionic tissue (Arias-Stella) were seen in some cases.

It appears that cellular infiltration, necrotic changes, or squamous metaplasia are a direct effect of the ring, since these are all more common and intense in tissue in contact with the device. However, these do not indicate serious pathology, since all our patients were clinically normal and without symptoms. The three cases showing squamous metaplasia, followed for four months to two years, revealed no abnormal findings. The most likely explanation would seem to be a foreign body reaction, which could be partly responsible for the effectiveness of the ring.

Design of Intra-Uterine Contraceptive Devices

Determination of the size of the endometrial cavity *in vivo*: two techniques

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A simple technique was devised for measuring uterine cavity size *in vivo*. A hysterogram was taken on patients in whom an intra-uterine bow was previously inserted. An injection of 1/2 to 3/4 ml. of ethiodol was made to mark the position of the bow within the uterine cavity. The uterus was then filled with 4½ ml of dye. The size of the device and of the cavity was then determined from the X-ray film. Since the actual size of the device was known it was possible to set up a simple proportional equation to determine the actual size of the uterine cavity. The fundus varied from 30 mm to 50 mm. (The latter was in a puerperal uterus.) A less accurate but simpler technique was devised using the width of the endometrial cannula as a measure of distortion of the uterine cavity size. In a series of 100 hysterograms done on non-puerperal patients the width of the fundus was found to vary from 16 to 59 mm. The average width was 33 mm. The endometrial cavity length varied from 16 to 67 mm. The average length was 34 mm. Using the simpler technique the uterine cavity size was generally found to be about 75 to 80 percent of the apparent size as measured on the X-ray plate. The techniques described are suggested as a means of controlling the design of intra-uterine devices for experimental use.

Experimental intra-uterine devices: retention and reactivity

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Several different materials and shapes of intra-uterine devices were used to find an innocuous material which would best be retained. Ninety-five insertions were made on 87 unselected patients. Stainless steel and two inert plastic materials were tested. Reactivity was checked by endometrial biopsies. Device position was determined by radiography.

A plain *Silastic* ring (2.2 cm diameter small, and 3.2 cm large) was first used. Only one patient in the entire series developed histologic endometritis, which followed the third insertion and third expulsion. The expulsion rate was 29 percent. When the outer edges of the device were altered from round to flat, with grooves placed in the circumference, expulsion rate was 24 percent. When another inert plastic, polyvinyl chloride, was used, the percentage of expulsions and endometritis was the same.

Plain stainless steel coils, coated with polyvinyl chloride to retain the inert characteristic, were evaluated. Although similar to Stone-Hall rings, several changes were made: the diameter was increased to 2.5 cm. Flexibility was increased to permit snapping back to the original shape. The coil was opened to allow more gripping surface and to increase elasticity. After 11 insertions, there have been no expulsions or foreign-body reactions. No relation between parity and retention of the ring was noted.

X-rays were taken in over half the patients. The ring was usually found in a transverse position, but could vary to vertical with all positions in between. Some sat directly over the internal os, others were found to be high in the fundus.

The use of larger Lippes loops: preliminary report

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The Lippes loop is a very satisfactory intra-uterine contraceptive device, but the smallest size has rather high expulsion and removal rates. Dr. Lippes has reported that lower expulsion, removal, and pregnancy rates are obtained with loops of larger size than the No. 1 (25 mm diameter), which is the size used in the medical follow-up study in Taichung reported at this conference by Lee and Wei (page 23). Accordingly, a comparative study of three larger sizes of loop was begun in May 1964. Designated as loops No. 2, 3 and 4, these loops have diameters of 31 mm, 30 mm, and 27.5 mm respectively.

A total of 404 insertions was made from May 15 to July 31 and 343 cases (85 percent) were successfully followed up during August. Although it is premature to draw any solid conclusions from analysis of the results so far obtained with the relatively small number of cases observed with each size, preliminary tabulations show a combined expulsion and removal rate of 1.7 percent at one month after insertion, which may be compared with the rate of 6.1 percent for loop No. 1 at one month. The No. 3 loop (30 mm) seems to be particularly suited for use by OBG practitioners; it is not difficult to insert and the discontinuation rate is low. The study is being continued.

Comparative study of two intra-uterine contraceptive devices

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Alternate insertions were made of 150 Lippes loops (large), which are made of polyethylene and have a cervico-vaginal appendage, and 136 stainless steel Hall-Stone rings, which are strictly intra-uterine. The advantages and shortcomings of both devices are compared.

Pregnancy rates per 100 cases were 4.4 for the loop, and 6.3 for the ring. These rather high pregnancy rates may be ascribed to the fact that we increased our patients' fertility by premedication with *Enovid*, and to our 100 percent follow-up, by which every single case of pregnancy is known to us.

The rates for *expulsion* were about equal for the two devices: 14.8 for the loop, 16.4 for the ring.

Removals for medical reasons were also about equally frequent for the two methods: 10.4 for the loop, and 12.3 for the ring.

It has been claimed that devices with an appendage extending through the cervical canal into the vagina produce a higher incidence of *infection* than strictly intra-uterine devices. At present, our clinical observations as well as our laboratory studies supply no evidence to support this theory. Our clinical findings show that the occurrence of major and minor infections is equal in loop and ring wearers. Also, both bacteriological studies and endometrial biopsies revealed the same low incidence of infection for both devices. These findings are still preliminary and must be confirmed by future clinical and laboratory observations.

Problems connected with *insertion* and *removal* of the two devices are discussed. While insertion of either device is usually a simple procedure, complications may occur. In our own series we had one incidence of perforation of the uterine wall following a loop insertion, and one case of severe hemorrhage, which necessitated hospitalization. Such incidents, although rare, support our opinion that the intra-uterine method should be handled by physicians, not by paramedical personnel. Even removal of the loop may present a problem. This is rare, while removal of the ring is generally more difficult, as our case histories show.

The importance of stiffness in intra-uterine contraceptive devices

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Because it is theoretically possible that the expulsion rate of intra-uterine contraceptive devices may be related to the stiffness of the device, tests were made to determine the modulus of elasticity of some devices. The test involves a measurement of the work done in placing a spring in tension in one plane, the spring in this case being the intra-uterine device. It was suspended with a string attached to each end; then weights were added to measure the tension in grams against the stretching in centimeters of the various devices. This "modulus" will of course vary with many things, e.g., the modulus of elasticity of the material itself, the shape of the device, and its cross-sectional diameter.

Tests were carried out on all four sizes of loop, the Margulies coil No. 5, and the Birnberg bow No. 3. It was found that the Margulies coil was straightened with 105 grams of force; Loop No. 1 with 155 g; Loop No. 2 with 565 g; and the Birnberg bow required about 605 grams to be straightened. Because expulsion of the devices usually takes place through a cervical canal of approximately 4 mm, the most significant figures appear to be the force needed to completely straighten each particular device. It is interesting that the "modulus" of the various devices correlates with the rates of expulsion. The stiffest device is the one which has the lowest rate of expulsion.

Clinical study of tailed and non-tailed intra-uterine contraceptive devices

Peter B. SEGAL and Richard FRANK, *Planned Parenthood Association, Chicago Area*

An IUCD clinic was established within the framework of the clinical facilities and administration of the Planned Parenthood main center in Chicago. This service was offered only to regular patients of the clinics. Tailed (loop) and non-tailed devices (plastic bow and steel ring) were inserted only during menstruation or period of withdrawal bleeding or two months postpartum. This required the use of interval techniques and consultation in manipulation of the orals to produce withdrawal bleeding within the proper appointment time.

All metal instruments, including specula, dressing forceps, inserters, removers, tenacula, and uterine sounds, were autoclaved before use. Plastic equipment was cold-sterilized for 24 hours in 1:1000 *Zephiran* solution. The cervix was cleansed with 1:1000 aqueous *Merthiolate* and sterile disposable plastic gloves were used during the insertion procedure.

Patients were routinely checked after the completion of the first menses with the device *in situ* (usually four to five weeks after insertion), and at two-month intervals thereafter. In the case of the plastic bows and steel rings, the uterine cavity was probed at each check visit. In the period from January 1, 1964 to September 1, 1964, a total of 255 devices were inserted. There were three expulsions—two steel rings and a small loop; 22 devices were removed for various reasons. Six patients incurred signs and symptoms of pelvic inflammatory disease. Two patients experienced surgery referable to the IUCD. There were four pregnancies, all occurring with the small plastic bow *in situ*.

Use of a liquid silicone polymer for intra-uterine contraception

Frank SHUBECK, *Department of Obstetrics and Gynecology, University of Oregon Medical School, Portland, Oregon*

This is a preliminary report on our use of a silicone polymer, which readily polymerizes when mixed with a catalyst. The reaction, which is sufficiently complete within 10 minutes at room or body temperature, converts the liquid silicone material into a soft but firm resilient solid. The liquid plastic conforms to a uterine cavity of any size or shape, thus obviating the need for various sizes of preformed or pre-cast substances. A control series was established in which the silicone polymer was alternated with a Margulies spiral No. 5 whenever possible.

Mechanism of Contraceptive Action

Effect of intra-uterine contraceptive device on uterine motility

S.J. BEHRMAN, *Department of Obstetrics and Gynecology, The University of Michigan Medical Center, Ann Arbor, Michigan*

A new transducer has been developed, with a maximum outside diameter not exceeding 3 mm; it is temperature-stabilized to the human body and records absolute pressures. This transducer in its prototype has been used extensively throughout the menstrual cycle to study the variations of the norm throughout the various phases of the menstrual cycle as well as the immediate postpartum period. Currently, three of these transducers have been built into a Lippes loop in an attempt to record any peristaltic movement of the myometrium throughout various phases of the menstrual cycle. In addition, not yet in practical operation but almost completely built, there is a multichanneled electropotential unit which will be inserted into the uterine muscle transabdominally at the same time as the intra-uterine device is recording. Following this the intra-uterine device will be removed and the electropotentials alone will be read without the presence of a foreign body in the uterus. It is hoped that by extrapolation of concurrent recordings of intra-uterine pressures and intra-myometrial electropotentials, information will be obtained on the effect of an intra-uterine device upon myometrial activity.

Effect of intra-uterine silk thread suture on the fertility of rats

R.R. CHAUDHURY, *T.K. Tarah Biology Division, Ciba Research Center, Bombay, India*

The placement of a uterine suture in the rat is an efficient anti-fertility procedure which prevents implantation on the side where it is placed. We have found that gonadotropin content of the pituitary gland is not altered, the uterine suture has no effect on the estrus cycle, nor does it affect lactation or milk ejection. These facts, plus the fact that the device does not prevent implantation in the opposite horn, indicate clearly that the anti-implantation effect is not a central effect mediated by blocking the release of pituitary hormones. Our studies show that the presence of an intra-uterine thread does not alter the ability of a rat uterine horn to respond to oxytocin. Pharmacological studies are in progress to determine the effect of various substances on the uterine horn itself, and to see if the presence of the foreign body alters in any way the normal biochemistry of the uterine horn.

Effect of intra-uterine devices on gestation in rabbits

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The contraceptive effects of the following types of intra-uterine foreign bodies (IUFB's) have been tested in mature rabbits: 1) plastic, radio-opaque disks and rings varying from 5 to 10 mm in diameter, introduced atraumatically into the uterine horn through the cervix after incising the vagina; 2) sutures of braided silk inserted through the antimesometrial border of the horn and either a) stitched to its wall at both ends or b) with the cervical end hanging free in the uterine lumen, as used by Doyle and Margolis in the rat. The untreated contralateral horn served as control. Following recovery the animals, divided into three groups, were mated and laparotomized or autopsied after conception: Group A (seven does) between days 2 and 6 p.c.; Group B (18 does) between days 8 and 17 p.c.; and Group C (six does) at both days 10 and 27 p.c. Some rabbits were allowed to deliver then remated and examined during their second pregnancies.

Findings: Group A (days 2-6): Normally developed morulae and blastocysts were recovered from both experimental and control sides. Recoveries were slightly, but not significantly, lower on the experimental side. There was no evidence of increased tubal or uterine motility in horns fitted with IUFB's. *Group B (days 8-17)*: Nidation was significantly suppressed by all IUFB's, reduction varying from about 50 percent to 75 percent. The overall implantation rate

$$\frac{\text{number of implantation sites}}{\text{number of corpora lutea}}$$

for all experimental groups was 47.6 percent compared with 89.3 percent in control horns. Intraluminal sutures of the Doyle-Margolis (free-ending) type prevented implantation more efficiently than fully attached sutures and the other plastic devices. The IUFB's did not interfere with the distribution of blastocysts through the uterine horn. *Group C (days 10 and 27):* There was significantly higher fetal loss after day 10 p.c. in experimental horns than in control horns (87.7 percent compared with 17.1 percent, indicating that the effect of IUFB's is not confined to the stage of implantation but continues throughout pregnancy in the rabbit.

Experimental studies on intra-uterine contraception

Amiya B. Kar, *Division of Endocrinology, Central Drug Research Institute, Lucknow, India*

In order to study the effect on implantation, rats fitted with a silk suture in one horn according to the method of Doyle and Margolis[1] were subjected to the "delayed-implantation" procedure. No implantation was observed in the treated horn in any of the animals, whereas in the control horn implantations were consistently observed[2]. This was suggestive of an anti-implantation effect of the intra-uterine device.

An attempt was then made to look for clues for the mechanism of such anti-implantation effect in the luminal fluid which is a critical environment for the pre-implantation blastocyst after its migration into the uterus. Rats were fitted with a surgical silk suture in one horn as before on the day of ovariectomy, and after six weeks subjected to estrogen therapy. It was observed that the mean volume of the fluid in the treated horn was about 50 percent less than in the control horn. It was somewhat viscous with a grayish tinge as compared to the normal thin and opalescent fluid from the control horn. This seemed to be a dehydration effect because most of the biochemical constituents of the fluid (protein and non-protein nitrogen, lactic acid, total lipids, phospholipids, and free and ester sterols) underwent almost a twofold rise in concentration. There were larger numbers of leukocytes in the treated horn fluid, but there was no difference in pH of the fluid (8.3-8.4) from the two horns.[3]

Perhaps the most interesting change occurred in the protein pattern of the fluid, which was studied by paper electrophoresis with serum as control. It was observed that the fluid from the control horn showed two bands of low optical density: one corresponding to the region between the γ and β globulin and the other between the β and α globulin. The fluid from the treated horn also had these two bands but in much higher concentration. In addition, an albumin band was consistently observed. The albumin constituted the major fraction in the proteinogram of the treated-horn fluid and constituted as much as 52 percent of the total proteins as revealed by planimetry. The albumin probably leaked from the serum and contributed importantly to the viscosity of the fluid. A noteworthy effect of such a high percentage of albumin would be a rise in over-all osmotic tension of the fluid. Assuming a molecular weight of 68,000 for albumin, a representative sample of the fluid containing 3 gm. percent of this protein would exert an oncotic pressure of about 8 mm Hg. This, together with the osmotic pressure due to the elevated non-protein constituents, may expose the blastocyst to a uterine milieu with considerable dehydrating influence. The net result may be a total dissolution of the blastocyst before implantation.

Some unusual changes were also observed in the uterine tissue itself. Thus after ovariectomy the treated horn did not show the characteristic involutionary changes. The percentage of water was not increased appreciably in this horn after estrogen therapy, although growth of the serosa, muscularis and the endometrium was observed. The organ was also hyperemic. The epithelium was typically spindle-shaped at places but low cuboidal at others. Localized compression and erosion of the epithelium with desquamation of cells was noticed; in a few animals keratinized metaplasia of the epithelium was detected. Healthy as well as hyperplastic glands with cystic changes were present. Some of these features suggest an increased sensitivity of the uterus to estrogen.

Investigations were also carried out to examine whether the presence of a silk suture in the uterus disturbed ovulation through some feed-back influence on the ovary. Rats fitted with a silk suture in both uterine horns were subjected to PMS gonadotropin treatment. The ovaries responded with characteristic superovulation and luteinization, although their weight did not increase to the same extent as in normal rats injected similarly with PMS gonadotropin.[4] The uterus showed stimulatory changes and an increased sensitivity to estrogen in the presence of the device as indicated by a greater ponderal response. The endometrium contained hyperplastic and cystic glands. The stroma was infiltrated with leukocytes; in some animals substantial numbers were seen. The epithelium was compressed and eroded in places with desquamation of cells, presumably due to pressure exerted locally by the suture. In a few animals keratinized metaplasia of the epithelium was observed. There was, however, no decidua formation.

Likewise, rabbits subjected to an ovulatory dose of HCG responded typically in spite of the presence of a silk suture in one of the horns. There was no significant difference in the number of ova discharged by the two ovaries. These studies therefore indicate that an intrauterine device does not interfere with ovulation.

The effect of an intra-uterine device on histology and biochemical composition of the rat uterine tissue was investigated at different time intervals (25 and 200 days) after insertion. It was observed that the device did not evoke any acute changes in the uterus. However, its prolonged presence (200 days) caused keratinized metaplasia of the epithelium in 20 percent of the animals, and cystic glandular hyperplasia in 10 percent. The oxygen uptake rate was doubled in the treated horn but other biochemical constituents (protein and non-protein nitrogen, RNA, DNA, collagen, glycogen, lactic acid, alkaline phosphatase, 5-nucleotidase, total lipids, free and ester sterols, triglycerides, and phospholipids and its bases) did not show any noteworthy change.[5]

Breeding experiments carried out with rats at 25, 100 and 200 days after insertion of the device showed invariable absence of pregnancy in the treated horn but not in the contralateral one. Similar observations were made with rabbits. The removal of the suture led to pregnancy in the treated horn provided there were no gross abnormalities in the horn. Rats fitted with a suture during prepuberal life showed pregnancy only in the control horn in breeding tests during maturity. However, as in adult animals, removal of the suture led to pregnancy in both horns. This shows that the insertion of an intra-uterine device even during prepuberty effectively stops pregnancy in adult life but does not disturb the reproductive potential of the animal.

The effect of an intra-uterine device on the fetus was investigated in rats. A silk suture was inserted in one of the uterine horns as before during the early (day 8) or late (day 17) stages of pregnancy. This procedure had no adverse effect on the fetus or the number of offspring born. The duration of pregnancy was not disturbed and there was no evidence to indicate that it caused abortion. No noteworthy ponderal, histological, or biochemical changes (nitrogen, RNA, alkaline phosphatase, and glycogen) were evoked by the device in the postpartum uterus.[6]

There was no evidence of a disturbance in sperm passage through the genital tract of rats and rabbits fitted with a silk suture. Preliminary pharmacodynamic studies in rabbits, involving simultaneous *in vivo* kymographic recording of the uterus, did not show any consistent suppressive or stimulatory effect of an intra-uterine device on myometrial contractility.

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Action of intra-uterine foreign bodies in the rat and rabbit*

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Since the revival of interest in the intra-uterine contraceptive devices in recent years, several experiments to demonstrate the effectiveness and mechanism of action of such devices have been performed on laboratory animals. Owing to our special interest in mammalian fertilization, we have inserted cellophane tubes containing oil, paraffin spindles, millipore filter soaked with oil, cotton threads soaked with various oils, etc. into the rabbit uterus. So far, none of these foreign bodies has shown any effect on fertilization. The following experiments, however, were performed to determine (1) the time of the removal of the foreign body in relation to implantation and the decidual reaction in the rat, (2) the effect of the intrauterine foreign body on the transportation, implantation, and development of embryos in the rabbit, and (3) the differential reaction of the foreign body between the rat and rabbit.

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Methods

Virgin Sprague-Dawley rats (200 g) at random stages of estrus cycle were fitted with braided silk thread (size 6-0) extending through the complete length of the uterine lumen, and piercing the anti-mesometrial wall just above the cervix and just below the uterotubal junction. In each animal, one uterine horn, allocated at random, received the thread and the other served as control. Fourteen days later, the rats were placed with normal or vasectomized males and examined each morning for the occurrence of mating (day 1). Groups of animals were killed between 9 and 10 a.m. on day 4 or day 5 for the recovery of eggs, or on days 12 to 18 for the examination of embryos.

In other groups of rats, the thread was removed between 9 and 10 a.m. on day 2, 3 or 4 of pregnancy, using aseptic technique and ether anesthesia. The rats were then examined on day 12 to ascertain the occurrence of pregnancy, the number of implantations, and the development of embryos.

The thread was similarly removed from the rats which had been mated to vasectomized males. A second operation was performed between 9 and 10 a.m. on day 5, and both uterine horns were traumatized with artery forceps at five points along their length. The rats were killed on day 8 between 9 and 10 a.m., and the uterine horns were carefully examined and weighed for the assessment of the decidual cell reaction (DCR).

For the rabbit experiments, mature animals after 3 weeks' isolation were fitted with braided nylon thread (size 0), entering the lumen of the uterus about 5 mm below the uterotubal junction and leaving about 5 mm above the cervix. In each animal, one uterine horn, at random, received the thread and the other served as control. Fourteen days later the animals were artificially inseminated and induced to ovulate by an intravenous injection of 50 I.U. of HCG. At 72, 120, and 168 hours (14 days) after the estimated time of ovulation, the animals were killed and the uterine horns were flushed for the recovery of eggs or examined for developing embryos. Removal of the thread was performed at 120 hours after ovulation in a few animals and they were examined on the 14th day of pregnancy.

Results

Our preliminary observations in the rat agreed with the published work of Doyle and Margolis and implantation was not observed in uterine horns containing a thread. Normally developing fertilized eggs could be recovered from the fallopian tubes on day 4, but on day 5 normal blastocysts were only found in the control horn. A variable amount of debris, with a high leukocyte content, was flushed from the experimental uterine horn on day 5. These observations, supported by the results of Schuchner and Davidson, show either that egg transport through the uterus was abnormal, or that all the eggs degenerated soon after reaching the uterus. In a series of 55 rats it was found that the ovaries on the control side had a mean of 6.76 corpora lutea (±0.31) after mating, whereas these on the experimental side had 5.82 (±0.25). The difference is significant ($p < 0.02$) and agrees with the observations of Zipper, Delgado and Guiloff, who used the same strain of rat. This may be explained by an effect of the intra-uterine thread in disturbing the ovarian blood supply on the experimental side.

Table I presents the results when the thread was removed on day 2, 3, or 4. Implantation was slightly affected (62 percent vs. 93 percent) after removal of the thread on day 2, but was completely inhibited (0 percent vs. 91 percent) after removal on day 4. Similarly, Table II shows a severe inhibition of the DCR if the thread was not removed, or removed on day 4, but only a slight inhibitory effect if the thread was removed on day 2.

TABLE I

Effect of removal of the IUFB on pregnancy in the rat
Eight animals in each group, examined on day 12 of pregnancy

Removal on	*Control uterine horn*				*IUFB uterine horn*			
	Number females pregnant	Total corpora lutea	Total conceptuses	Develop.	Number females pregnant	Total corpora lutea	Total conceptuses	Develop.
Day 2	7	59	55	93%	6	45	28	62%
Day 3	7	58	45	78%	2	46	9	17%
Day 4	8	53	48	91%	0	42	0	0%

TABLE II

Effect of removal of the IUFB on the decidual reaction in the rat
Eight animals in each group, traumatized on day 5 and examined on day 8 of pseudo-pregnancy

Removal on	*Control uterine horn*		*IUFB uterine horn*	
	Mean uterine wghts. (mgs. ± s.e.)	No. of females with DCR > 400 mg	Mean uterine wghts. (mgs. ± s.e.)	No. of females with DCR > 400 mg
Day 2	804 ± 94	8	596 ± 80	6
Day 3	686 ± 66	8	477 ± 74	5
Day 4	572 ± 85	7	284 ± 32	1
IUFB in place	753 ± 79	8	336 ± 20	1

These results demonstrate a close association between the failure of DCR on the one hand, and the inhibition of implantation on the other. The foreign body is effective during the time of preparation for implantation, but not at an earlier time. Thus, it appears that some specifically timed local trigger mechanism, whether a biochemical substance or a neuro-endocrine reaction necessary for the initiation of implantation, was exhausted or used up by the presence of a foreign body. However, there is the possibility that the almost complete failure of implantation following removal of the thread on day 3 or 4, when normally developing eggs were found in the tube, may also suggest the induction of an embryo-toxic uterine environment by the foreign body, because the extent of the DCR after the removal on day 3 seemed sufficient to support implantation to a certain extent.

TABLE III

Effect of the IUFB on pregnancy in the rabbit

		Control uterine horn				*IUFB uterine horn*			
Examination (days after ovulation)	No. of rabbits	C.L.	Embryos	% Egg recovery	Normal embryos as % of eggs recov.	C.L.	Embryos	% Egg recovery	Normal embryos as % of eggs recov.
3	4*	21	10 early blast. 3 deg. eggs	62	77	20	9 early blast. 1 deg. egg	50	90
5	5*	27	21 blast. 2 deg. eggs	85	91	31	22 blast. 1 deg. egg	74	96
7	5	19	17 swellings in 5 animals	90	100	33	8 swellings in 3 animals 16 deg. blast.	73	33
14	5	35	28 concep. in 5 animals	80	100	28	4 deg. concep. in 2 animals	14	0
14 (removal of IUFB 5 days after ovulation)	3	19	15 normal and 2 abn. concep. in 3 animals	90	88	13	9 normal concep. in 2 animals	69	100

* One degenerating blastocyst was recovered from the vagina of one animal.

The results for the rabbits are presented in Table III, which shows that fertilized, normally developing eggs can be found in the fallopian tubes or uterine horns in the presence of thread up to seven days after ovulation, although the number of eggs recovered from the treated side was slightly lower than the control side. However, a higher proportion of blastocysts had degenerated by the time of implantation (on day 7) or soon after. Contrary to the observations made in the rat, degenerated embryos were observed on day 14, showing that in the rabbit the presence of a foreign body also causes death of embryos after implantation. The presence of normal embryos in two animals following the removal of thread on day 5 again indicates that the inhibition of implantation would not occur if the foreign body was removed two days before implantation.

The mean diameters of the blastocysts recovered from the control and experimental horns five days after ovulation were respectively 1.76 (± 0.1) mm and 1.67 (± 0.1) mm, and they were all morphologically normal. In 33 rabbits there was no significant difference in the number of ovulations occurring from the control and experimental ovaries, the means being 5.2 and 5.5 respectively. It appears that rabbit blastocysts may survive for more than three days in the presence of thread and that implantation can also occur, but that the embryos may subsequently degenerate. This may provide evidence that the intra-uterine foreign body interferes with the continuing endometrial normal function in the rabbit rather than induction of some specific uterine environment, as in the rat.

Discussion

It is to be expected that the action of the intra-uterine foreign body may vary amongst the different species. Apart from the possible disturbance of the cycle of ovarian activity in the cow, reported by Hawk *et al.* in this conference, no detailed observations on ovarian activity have been made in laboratory animals or other species.

Concerning the effect on fertilization, our observations on the rat, rabbit, and mouse (unpublished), and the reports from others, do not support the view that fertilization is inhibited. Even in the human, a newly penetrated pronuclear egg with fertilizing sperm tail has been presented at this conference by Bonney and Cooper. The monkey egg with corona radiata and cumulus, mentioned by Mastroianni, is probably a newly ovulated egg, either recently penetrated or with insufficient time to have been fertilized. The presence of corona radiata and cumulus is not necessarily an indication of failure of fertilization.

As for the disturbance of egg transport, the work by Mastroianni *et al.* on monkeys, Hawk *et al.* on cows, Doyle *et al.* on mice, and our work on rats and rabbits, all indicate a certain amount of disturbance with egg transport by the presence of an intra-uterine foreign body.

The main effect of the intra-uterine device, however, is on implantation; but again, the mode of action varies between different species, such as the rat, the rabbit, and other species reported in this conference.

Since there is evidence that the intra-uterine device does disturb egg transport and that its effect is not confined to the stage of implantation but continues through pregnancy, as shown in our observations and in those of Eckstein and Adams, it would be of interest to explore all these possibilities and other effects in all laboratory animals.

Summary

The action of an intra-uterine foreign body was studied in the rat and rabbit. Insertion of various materials into the uterine horns of rabbits has so far not inhibited fertilization.

Although egg transport may be disturbed by the foreign body, implantation was prevented in the rat whereas in the rabbit normal blastocyst development and implantation could occur.

Following removal of the foreign body at different days after mating or during pseudopregnancy in the rat, it appears that (1) the inhibition of implantation by the presence of the foreign body is closely associated with the inhibition of the decidual reaction, (2) the greatest effectiveness of the foreign body is during the time of preparation for implantation, and (3) interference with a specific event essential for implantation occurs. Further comparative study of the mode of action in different species is urged.

Studies on mechanism of action of intra-uterine foreign bodies in rodents

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Carleton and Phelps showed that if an IUCD was restricted to either end of the long rabbit uterus, then normal pregnancy could occur at the other end. This indicates that the IUCD prevents the implantation of normal blastocysts, and that it can do so only in a localized region around itself. One possible hypothesis to account for this action may be stated briefly as follows: The IUCD causes stretching of the myometrium. The stretched smooth muscle cells are depolarized, thus increasing the rate at which spontaneous action potentials occur. This increased electrical activity leads to increased contractile activity (motility). The electrical and mechanical activity are propagated because of the syncytial character of smooth muscle, and this is under hormonal regulation. Finally, it may be supposed that excess uterine motility would prevent implantation. This hypothesis was tested in two ways.

1. If stretched smooth muscle cells are the adequate stimulus for intra-uterine contraception, then a ligature around the uterus, tight enough to cause deformation but not so tight as to occlude the lumen, should prevent pregnancy. Such a thread was tied around one horn of the rat uterus in ten animals. These animals became pregnant on the test side in spite of the thread.

2. For a more conclusive test of this hypothesis, the rat uterus was stimulated electrically at the time of normal implantation. If an IUCD works because it provokes excess electrical activity, then the introduction of excess electrical activity via a chronically placed stimulating electrode should also prevent pregnancy. This was accomplished as follows: Normal rats were mated and the day sperm were found in the vagina was designated day [illegible]. On day 3, one electrode was placed on each horn of the uterus at the ovarian end. An indifferent electrode was secured under the skin, out of contact with skeletal muscle. On the morning of day 5 the rats were placed in specially made plastic restraining cages and stimulation of one of the uterine electrodes was begun. This continued uninterrupted for 72 hours. The stimulation program consisted of a ten-second train of pulses repeated every two minutes. The ten-second train contained 100 pulses, each 80 msec. wide. The total current flowing through the electrode on the uterus was monitored, and was in all cases greater than 1 ma for at least 48 hours. A rough calculation shows that 1 ma should produce a current density in the myometrium adequate to cause electrical excitation. In estrous animals, using this stimulation program and visual observation, vigorous contraction is produced with only 0.1 ma. Rats tolerate this experiment quite well. In a series of animals, essentially normal pregnancies occurred in both the stimulated and unstimulated horns. It seems unlikely that an IUCD prevents pregnancy by provoking excess electrical activity.

Present research is concentrated upon the autonomic nervous system with respect to its possible involvement in the mode of action of intra-uterine foreign bodies.

Effect on rat pregnancy of an intra-uterine silk thread

Elsa B. SCHUCHNER and Oscar W. DAVIDSON, *The Population Council, Rockefeller Institute, New York City*

Unilateral insertion of a silk thread into the uterine cavity did not interfere with normal cycling in the rat as shown by vaginal smears. When the thread was placed *in situ* for at least three cycles prior to mating, pregnancy was prevented in the experimental horn, while no effect could be observed in the control horn. The removal of the device on day 10 of pregnancy did not interfere with delivery, postpartum ovulation, or subsequent pregnancy. This effect was obtained regardless of the position of the inserted thread (upper, lower, or middle third of the experimental horn). When the device was inserted after mating, the effect depended upon the stage of pregnancy and the position of the device in the uterus. Insertion of the thread in the upper third of the experimental horn during any of the first four days of pregnancy partially prevented implantation. Fitting of the device in the middle or lower third of the horn during the preimplantation period had a less noticeable effect, but the average number of implantation sites was lower than in the control horn. These animals were mated again with the device *in situ* and no implantation sites could be found in the experimental horn. Egg recovery was attempted in animals bearing the device for at least two weeks before mating. The number, distribution, and morphology of the recovered zygotes up to day 3 of pregnancy was comparable in both tubes and was within the range observed in normal females. On day 4 the number of eggs recovered from the experimental uterine horn was below the average of the control side. This difference was more noticeable on day 5, when the experimental horn showed a fourfold decrease compared to the control side.

The effect of the intra-uterine contraceptive coil on the oviducts

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Tubal insufflation and kymogram recordings were made on ten patients prior to the insertion of an intra-uterine coil. Approximately one month after the coil was inserted, repeat insufflations were performed. There were no significant changes in the kymogram, and the tracings obtained in our study were indistinguishable from a normal pattern. Cervical escape of gas did not present a difficulty. The insufflations were done at approximately the same time in the cycle. Thus the contraceptive feature of intra-uterine devices is not apparently due to tubal spasm or mechanical obstruction at the cornua. No conclusion can be drawn about tubal peristalsis inasmuch as uterotubal insufflation with carbon dioxide cannot be sufficiently interpreted to read accurately moderate increases or decreases in tubal activity.

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